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*Gold & De Graff, Jour. A. M. A., March 31, 1928.

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THE

AMERICAN JOURNAL

OF THE MEDICAL SCIENCES

DECEMBER, 1928

ORIGINAL ARTICLES.

THE RELATION OF BLOOD SUGAR TO BLOOD PRESSURE.*

By Herman O. Mosenthal, M.D.

NEW YORK

(From the Department of Medicine, New York Post-Graduate Medical School and Hospital.)

Neubauer, in 1910, noted the frequent relation between hypertension and hyperglycemia. Since that time, this subject has been discussed frequently. Some authors (Maranon, Tachau, Kylin, Härle, Botti, Hagelberg, Herrick, Williams and Humphreys, Hopkins, Bierry, Hitzenberger and Richter-Quittner, Oppenheimer and Fishberg) agree with Neubauer, while others (Rosenbloom, Mohler, Iwai and Löwy, Stilling, Kahler, Koopman) do not believe that the association of increased blood sugar and an elevated arterial tension is a common one.

The underlying impressions in regard to cause and effect of this frequent, if inconstant, concurrence of elevated glycosuria and arterial tension are extremely vague. There has been a feeling of uneasiness concerning it because of the severe effects a permanent hypertension entails and since many clinicians are regarding a high blood sugar as a messenger of ill omen, foreboding, arteriosclerosis, furunculosis, cataract and other degenerative and infectious lesions.

After it had become known that epinephrin could raise the arterial pressure, and it had been established that this internal secretion mobilized glucose from glycogen, and could thus elevate the blood sugar, Neubauer correlated these two facts and ascribed the simul-

* Read before the Association of American Physicians, Washington, D. C., May, 1928.

taneous occurrence of hypertension and hyperglycemia to this common cause. Theoretically, this may be possible; from the experimental and clinical viewpoint, it lacks confirmation. This idea has been categorically denied and affirmed by any number of observers, but definite proof of an excessive activity of the suprarenal gland has not been furnished. The very presence of epinephrin in the blood has, thus far, not been demonstrated and the successful quantitative estimation of this substance has not been accomplished.

Oppenheimer and Fishberg, after a review of the literature and their own experiences, come to the conclusion "that there is considerable anatomic evidence that hyperplasia (and cortical adenomata) of the suprarenal glands is a frequent concomitant of arterial hypertension."

It is interesting to note that this situation has other possibilities that may complicate the relationships of the suprarenal gland, blood pressure and blood sugar. Wilder makes a report that during hypoglycemic coma, the systolic pressure rose as high as 220 in a man whose arterial tension usually did not exceed 120. This rise in pressure is attributed to the liberation of epinephrin, a spontaneous attempt at the restoration of normal blood sugar. This injects a new factor into the situation inasmuch as the cause for the symptom complex under discussion may originate in a change in the blood sugar as well as in abnormal secretion of epinephrin.

Concerning the diminution of epinephrin in the blood and its effect, we can speak with a little more assurance for it is generally appreciated that in Addison's disease, hypotension and a lowered blood sugar are characteristic. In conclusion, it may be said that the cases of suprarenal tumors reviewed by Oppenheimer and Fishberg furnish evidence of the probability that epinephrin may be responsible for the coëxistence of hypertension and hyperglycemia. It is not plausible, from the available evidence, that this applies to more than a very limited and exceptional number of instances of essential hypertension.

The overactive thyroid gland has been regarded as a factor in producing this symptom complex. However, the character of the blood pressure in hyperthyroidism with its slight rise in systolic pressure and comparatively high pulse pressure, usually ascribed to increased cardiac output, accompanying the elevated basal metabolism, is so different from that in cases of essential hypertension, under consideration here, as to put them in a different clinical category; though it must be recognized that certain blood pressure and blood-sugar changes accompany hyperthyroid activity.

There are other internal secretions that may have a bearing upon this problem of the association of hypertension and hyperglycemia but the possibility of their being involved in the production of the routine case of hypertension is even more remote than that of suprarenal or thyroid gland.

Another aspect of this question, is whether hypertension may not be the cause of hyperglycemia. Directly there is no relation of cause and effect; this can be readily appreciated from some of the authors already quoted who were unable to demonstrate a blood sugar above the normal in hypertensive patients. However, this may occur indirectly through the development of an arteriosclerosis. Clifford Allbutt was one of the first clinicians to appreciate the true course of events regarding hypertension and arterial changes. He placed the former as preceding the latter, thus recognizing the fact that a persistently elevated blood pressure entails arteriosclerosis (whereas a primary arteriosclerotic state does not bring about an elevation of blood pressure). Many observers have verified this fact until today it is recognized that the arteries throughout the whole body are involved by the morbid process. In this net of disease, the pancreas is frequently implicated. It is upon this idea that O'Hare, Kylin and Botti, when they find a diminished carbohydrate tolerance in hypertensive patients, base the statement that these are instances of pre-diabetes, that is, of incipient pancreatic lesions. The increased blood glucose found in some cases of essential hypertension may be ascribed to this cause. Joslin, to a certain extent at least, concurs in this idea when he says that arteriosclerosis may play an important rôle in the production of diabetes.

The relation of overindulgence in starchy food, obesity, hypertension, arteriosclerosis and a high blood sugar has been stressed by Herrick as a definite clinical entity. Joslin and Emerson and Larimore have shown how the sedentary, high-calory feeder is prone to suffer from diabetes. It has become very popular to assume that the obese individual is prone to hypertension; this is undoubtedly true, but not to the extent usually entertained, since Symond's extensive statistics for all ages show a systolic pressure of but 134.4 for the obese, as compared to 126.9 for normals. Herrick's overweight patients show a definite reduction of blood pressure when the blood sugar is reduced; this he claims does not occur in individuals who are of normal or underweight. It would appear that overindulgence in food could be responsible for a combined hypertension and hyperglycemia.

Granting the probability that disturbed internal secretions (notably suprarenal and thyroid) and overindulgence in food may result in a state of heightened blood pressure and blood sugar and that hypertension, by causing arteriosclerosis of the pancreatic vessels, may result in hyperglycemia, there remains the possibility that the change in the blood sugar may, at times, be the primary factor in the situation. The diabetic would be the ideal patient upon whom to study this problem. There have been innumerable investigations of this question and the results are most confusing. Thus Kylin claims to find the blood pressure of the diabetic increased

while Rosenbloom does not; Janeway, in 1904, anticipated the succeeding generation when he found that the obese diabetic was prone to exhibit hypertension while his malnourished brother did not; Joslin's statistics appear to show a somewhat elevated value for blood pressure in older diabetics. This phase of the problem, namely, the possible causation of hypertension through the influence of hyperglycemia, has been studied for the past few years by obtaining blood-pressure readings in routine fashion whenever blood-sugar determinations were made.

The influence of hyperglycemia may be investigated under two headings: the immediate result upon blood pressure and the outcome of prolonged sugar elevation.

The relation of blood pressure to a temporary increase in blood sugar may be readily studied during the course of sugar-tolerance tests; in carrying these out the blood sugar and blood pressure were determined on fasting and twenty, forty, sixty and one hundred and twenty minutes after the administration of 100 gm. of glucose. Tables I and II give the details of the procedure. Table I is of a man whose blood-sugar curve is normal, while Table II is an example of diminished carbohydrate tolerance. In neither case does the blood pressure parallel the fluctuations in the blood sugar.

TABLE I.—CONSTANT BLOOD PRESSURE WITH VARYING BLOOD SUGAR.

Time, A.M.	Blood pressure.		Blood sugar, mg. per 100 cc.	Remarks.
	Systolic.	Diastolic.		
9.10	124	80	97	Fasting.
9.15	...	..	...	100 gm. glucose by mouth
9.35	122	82	136	
9.55	122	80	130	
10.15	120	80	107	
11.15	121	82	94	

Sugar-tolerance test on M. E., male, aged twenty-seven years.

TABLE II.—CONSTANT BLOOD PRESSURE WITH VARYING BLOOD SUGAR.

Time, A.M.	Blood pressure.		Blood sugar, mg. per 100 cc.	Remarks.
	Systolic.	Diastolic.		
9.30	110	72	156	Fasting.
9.40	...	..	...	100 gm. glucose by mouth.
10.00	108	66	247	
10.20	108	68	290	
10.40	110	62	308	
11.45	104	64	333	

Sugar-tolerance test on E. A., female, aged thirty-two years.

Table III gives a summary of all the tests carried out; in no instance does the arterial pressure rise though a marked increase in the blood sugar often occurs.

TABLE III.—HIGHEST AND LOWEST BLOOD SUGARS AND CORRESPONDING BLOOD PRESSURES OBSERVED IN 31 GLUCOSE TOLERANCE TESTS. (FIVE BLOOD-SUGAR AND BLOOD-PRESSURE READINGS IN EACH CASE.)

	At lowest blood sugar.		At highest blood sugar.			At lowest blood sugar.		At highest blood sugar.	
	Blood pressure.	Blood sugar.	Blood pressure.	Blood sugar.		Blood pressure.	Blood sugar.	Blood pressure.	Blood sugar.
1	110/72	156	104/64	333	17	128/74	153	118/64	300
2	137/76	117	112/60	344	18	118/75	111	95/64	166
3	104/66	100	111/58	153	19	119/80	96	120/82	145
4	126/78	181	126/67	333	20	130/88	111	113/68	181
5	126/84	100	104/65	222	21	130/92	110	132/90	185
6	108/68	95	118/68	200	22	98/62	83	104/62	120
7	97/50	80	94/52	111	23	124/74	117	128/90	241
8	121/82	94	122/82	136	24	138/92	100	128/87	111
9	112/78	108	108/70	230	25	99/69	111	106/64	250
10	94/60	83	96/64	100	26	124/76	111	114/69	134
11	134/82	79	128/78	143	27	108/56	111	106/58	133
12	122/78	125	122/74	300	28	114/76	129	109/70	243
13	148/92	133	134/83	339	29	104/60	101	112/70	235
14	132/80	119	126/78	260	30	111/74	166	116/79	250
15	119/81	111	119/80	250	31	114/86	71	114/82	172
16	94/64	100	95/57	133					

There is no rise of blood pressure paralleling the increase of blood sugar in any of the tests.

It may, therefore, be concluded that over brief periods of time a rise in blood sugar causes no change in the blood pressure.

The following cases are all instances of diabetes mellitus that have shown a more or less persistent hyperglycemia over a number of years; the blood-pressure observations were taken at the same time as the blood specimens; the blood was examined more frequently when the urine was sugar-free than when it contained sugar and, consequently, the blood-glucose readings represent the low rather than the high values for these patients. In none of the cases cited did the blood pressure rise in spite of the high blood sugar; in some a hypotension persisted throughout. These cases demonstrate that hyperglycemia, persisting as long as seven years, will not result in an increase of blood pressure.

Case Reports. CASE I.—H. C. C., female, aged fifty-one years, diabetes mellitus, observed from May, 1925, to October, 1927; approximately 30 to 50 pounds underweight during the period of observation, receiving insulin. One blood-sugar determination above 300 mg. per 100 cc., 28 between 200 and 300 mg., 8 between 150 and 200 mg., 2 below 150 mg.; 36 blood-pressure readings varied between 94/70 and 130/90 except one determination of 176/90.

CASE II.—C., female, aged forty-two years, mild diabetes mellitus, observed from September, 1920, to November, 1927. Thirteen blood-sugar observations of 200 mg. or over, 4 between 150 and 200, 4 under 150; blood-pressure varied from 88/57 to 116/72; approximately normal weight for height and age throughout.

CASE III.—M. G., male, aged fifty-six years, mild diabetes mellitus since 1905, he usually overeats, a small amount of sugar is constantly present in the urine, blood-sugar determinations since July, 1921. Fourteen blood-

sugar observations of 200 mg. or over, 6 between 150 and 200 mg., 4 under 150 mg.; blood pressure on two occasions 140/74 and 146/70, otherwise varied from 132/68 to 100/62.

CASE IV.—C., male, aged forty-eight years, severe diabetes mellitus, observed from January, 1922, to October, 1927; 50 pounds underweight at first, during last two years normal weight, receiving insulin. Twenty-three blood-sugar determinations of 300 mg. per 100 cc. or higher, 17 between 200 and 300 mg., 3 between 150 and 200 mg., 6 less than 150 mg.; blood-pressure readings varied between 80/62 and 118/78.

TABLE IV.—THE 2 HIGHEST AND THE 2 LOWEST BLOOD-SUGAR READINGS OF EACH YEAR AND THE CORRESPONDING BLOOD PRESSURE IN CASE V.

Date.	Blood pressure.		Blood sugar, mg. per 100 cc.
	Systolic.	Diastolic.	
1925 Mar. 21	130	92	285
June 24	108	69	105
July 8	100	70	250
Nov. 11	114	82	125
1926 Jan. 6	102	68	111
Mar. 30	108	68	200
June 9	102	66	200
Dec. 15	122	76	136
1927 Feb. 15	112	76	166
Mar. 15	118	74	174
May 16	112	74	133
Sept. 15	118	78	141

Case V.—J. S., aged forty-five years, mild diabetes mellitus, about fifty pounds overweight throughout, observed from March, 1925, to September, 1927, blood sugar and blood pressure noted regularly every two to four weeks. Eleven blood-sugar readings below 150, 36 above 150; 46 blood-pressure readings, 94/62 to 134/80.

TABLE V.—THE 2 HIGHEST AND THE 2 LOWEST BLOOD-SUGAR READINGS OF EACH YEAR AND THE CORRESPONDING BLOOD PRESSURES IN CASE VI.

Date.	Blood pressure.		Blood-sugar, mg. per 100 cc.
	Systolic.	Diastolic.	
1924 July 28	110	71	250
Sept. 22	99	64	222
Nov. 26	105	72	111
Dec. 4	96	64	125
1925 Jan. 21	99	69	153
April 9	98	69	111
May 25	90	54	250
July 15	96	68	111
Nov. 25	106	70	250
1926 Jan. 20	104	70	250
Mar. 3	112	68	250
June 23	94	58	125
Dec. 15	92	66	138
1927 Feb. 15	98	64	220
Mar. 15	100	70	167
May 16	113	74	203
Aug. 12	104	76	167

Case VI.—H. S., aged forty-nine years, mild diabetes mellitus, about twenty pounds overweight throughout, observed from July, 1924, to October, 1927, blood sugar and blood pressure noted regularly every two to four weeks, 16 blood-sugar readings below 150, 43 above 150; 59 blood-pressure readings, 86/58 to 116/80.

TABLE VI.—BLOOD-SUGAR AND BLOOD-PRESSURE DETERMINATIONS IN CASE VII.

Year.	No. of blood-sugar determinations.			Blood-pressure determinations.			
				Lowest.		Highest.	
	200 mg. or over.	150 to 200 mg.	less than 150 mg.	Systolic.	Diastolic.	Systolic.	Diastolic.
1921	..	..	7	98	64	116	72
1922	10	5	11	92	58	114	78
1923	15	4	4	92	58	108	76
1924	8	4	4	82	58	110	66
1925	5	4	2	88	52	104	76
1926	8	3	0	86	58	104	78
1927	5	1	0	86	..	112	57

Case VII.—Male, aged fifty-four years, diabetes mellitus since 1921, observed since 1921, disease mild originally, now severe, about twenty pounds underweight throughout.

These figures cover a period up to seven years only. Joslin, Kylin and Koopman have stressed the fact that it is the older diabetic patient, rather than the younger one, who exhibits an elevated blood pressure. It may be that a hyperglycemia prolonged for ten, fifteen or more years will have a tendency to be accompanied by a hypertension.

Lest the relation of blood sugar to blood pressure as presented thus far is considered to cover the whole subject, it is desired to add a word concerning other effects a hyperglycemia may have and its importance as a guide to therapy. It is generally appreciated that the older diabetic is subject to skin infections, arteriosclerosis and its complications, notably gangrene of the lower extremities, and cataract. It has been taken for granted that such complications are due, in large part, to an elevated blood sugar. The very fact that they occurred in diabetic patients has been accepted as conclusive evidence on this point.

Herrick believes that a hyperglycemia results in arteriosclerosis, even in juvenile diabetics; Mohler accredits such vascular changes to the accompanying obesity; Joslin believes high-fat diets may be responsible for premature arteriosclerosis, while hyperglycemia does not seem to him to be a cause of the condition.

There is certainly some factor in the diabetic which favors vascular degenerations. They are more prone to occur in the protracted cases of diabetes. It has always seemed to the writer that they were most common in cases that had been the victims of inadequate treatment for ten to fifteen years. That is during this interval they had had glycosuria and polyuria. This transcribed into its pathological sequence would be: hyperglycemia, glycosuria, polyuria which entailed desiccation. The excessive dryness of the body continued over a long period might well affect the tissues adversely and be responsible for the arteriosclerotic changes. The elevated blood sugar would be the indirect cause of the diabetic complication under these circumstances.

There are some very interesting and suggestive experiments of S. Weir Mitchell on record which show that an excess of sugar in the circulation and desiccation both play a distinct part in the production of cataract in frogs. In these animals an excess of sugar injected resulted in cataract formation; the cataract was healed or prevented if the frogs were immersed in water; desiccation alone did not result in cataract formation. Consequently, the conclusion was reached that sugar in excess was a toxic influence.

Conclusions. An excess of sugar in the blood will not result in an increase in blood pressure over short periods of time and will not do so, as far as a limited clinical material permits the deduction, for a period of seven years. This does not exclude the possibility that a hyperglycemia in itself and indirectly, by inducing desiccation through polyuria, may not have a toxic influence favoring the development of such conditions as arteriosclerosis and cataract.

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THE TREATMENT OF DIABETES INSIPIDUS WITH PITUITARY POSTERIOR LOBE EXTRACT APPLIED INTRANASALLY.

By John R. Campbell, Jr., M.D.,

and

Herrman L. Blumgart, M.D..

Boston, Mass.

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The necessity for repeated hypodermic injections of pituitary posterior lobe extract in patients with diabetes insipidus has stimulated investigators to devise some other method of administration, less painful and more convenient. In 1922, one of us[1] demonstrated that pituitary posterior lobe extract, when applied intranasally checked both the polyuria and polydipsia as effectively as hypodermic injection. As was then pointed out, the success of the method in the patient studied may have been due to the small amount of pituitary extract he required, 0.005 cc. of pituitrin "O,"* subcutaneously being sufficient to control his symptoms. Since the original publication, no comprehensive clinical evaluation of the procedure has appeared in the literature. The results of such a study of 8 consecutive patients with diabetes insipidus are presented below.

Methods. Two intranasal methods are feasible. In one, from 0.5 to 1 cc. of pituitrin "O" is placed in an atomizer and sprayed into the nose so as to be deposited mostly on the roof of the nasopharynx. This is best done by inserting the atomizer nozzle at least half way up the nostril, and spraying slowly in the direction of the eyebrow.

* The pituitary posterior lobe extract used in this investigation was manufactured by Parke, Davis & Co. Pituitrin "O" (obstetrical pituitrin) is one-half the strength of pituitrin "S" (surgical pituitrin).

If the patient feels the pituitrin going over into the throat the nozzle should be tilted still higher. In order to insure getting all of the pituitrin out of the bottle, a small piece of rubber tubing may be attached to the collecting stem to prolong the latter down to the lowest point in the bottle. By this method, three, four, or six hour intervals have been allowed between treatments according to the antidiuretic effect obtained.

The second method is application by means of a cotton swab. A piece of ordinary absorbent cotton about the size of a Jordan almond is soaked with 0.5 or 1 cc. of pituitrin. Soaking of the cotton is conveniently accomplished by filling a 1-cc. glass syringe with the desired amount, poking the needle into the middle of the cotton, and discharging the contents of the syringe. Light squeezing will then evenly saturate the cotton and no pituitary extract will be lost. The pledget is lightly grasped with nasal forceps, and passed up one nostril in the direction of the eyebrow.

Difficulty is sometimes experienced in passing the middle turbinate bone, but can usually be obviated by worming the forceps a little and keeping the tips in close apposition to the nasal septum. It is sometimes necessary to push the middle turbinate bone gently aside with some such instrument as a smooth director, but it has never been necessary in our experience to make constant use of a nasal speculum.

In withdrawing the forceps, a director is held against the cotton to keep the latter from coming out too. One or two gentle prods fixes the cotton in place where it is left until the next application in four, six or eight hours. When in place, the lower end, just above the middle turbinate bone, can barely be seen. If the cotton is low in the nostril or on the pharnygeal side of the arch, little absorption of the pituitary extract will be obtained. Several careful trials must consequently be made at first to be sure the cotton is high up.

The patient soon knows better than the operator when the pledget is in good position against the roof of the nasopharynx, and can apply it himself. The pledget is left in place until time for the next application when it is easily removed by blowing the nose. As a rule, alternate nostrils are used. Where the nose is caked with crusts or thick purulent material, irrigations with physiologic salt solution will sufficiently cleanse the field for absorption.

Two principal complaints have come to our notice. There is an occasional burning sensation produced by the drug when first employed in the nose. This has always passed off after a few days. One patient, M. G., Case VII, experienced irritation of the nasopharynx after these studies had been completed and so treatment was temporarily discontinued. When one nostril is partially obstructed, slight difficulty in breathing is sometimes encountered. This usually ceases after both nostrils have been used a few times. None of the 8 patients had complete nasal obstruction on either side.

In order to eliminate as many disturbing factors as possible, all patients were studied under the following conditions:

1. Complete hospitalization with the privilege of getting out of bed part of each day.

2. A fixed salt and protein content of the diet. Variability in these factors has been shown to affect the output of urine. No food was allowed between meals, and all food given was eaten. Tea and coffee were withheld.

3. In some of the 8 cases a definite organic etiology for the diabetes insipidus was established. Patients in whom no definite organic lesion could be demonstrated did not respond to sterile water sprays and hypodermics.

4. All patients were encouraged to drink as much water as they pleased throughout the observations.

5. The fluid intake and urinary output were carefully measured, the specific gravity of the urine and the daily weight of the patient were measured.

Observations. The records and observations on the 8 patients with diabetes insipidus that have been studied are set forth below.

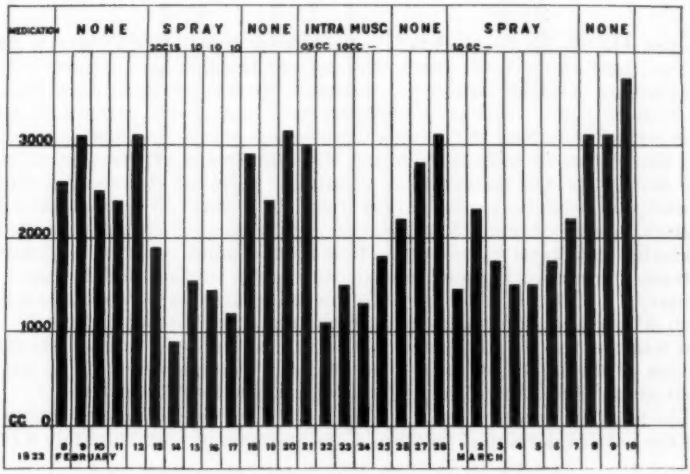

FIG. 1.—M. P., Surg. No. 16012 P.B.B.H. Black columns indicate fluid intake. 2/13 to 2/17 pituitary extract sprayed intranasally every four hours, first day 2-cc. doses, second day 1.5-cc. doses, and last three days 1-cc. doses. "Intramusc." 2/21 to 2/25 pituitary extract (obstetrical) every six hours intramuscularly in doses of 0.5 cc. first two days and in doses of 1 cc. last three days. 3/1 to 3/7 "spray" 1 cc. pituitary extract (obstetrical) sprayed intranasally every four hours.

Case Reports, CASE I.—M. P. (Hospital P.B.B.H., No. 32329, Surg. 16012), was a boy, aged thirteen years, weighing 50 pounds, who entered the hospital February 1, 1922, complaining of headache, vomiting, and failing vision. The past history and family history were not significant. One year before entry he noticed that he drank unusually large quantities of

water and that he passed urine frequently, getting up five to six times a night. Eight months before admission the headache became more severe and he suffered from vomiting and blurred vision. A right sided decompression was done three months before admission followed by a left sided decompression two and a half months before entry. Lumbar puncture three, and again two weeks before admission caused only transitory relief. Physical examination showed bulging of the bilateral decompressed areas, markedly impaired vision, bitemporal hemianopsia, and dilated and fixed pupils. Convergence of the eyes was normal but the other ocular movements could not be performed by the patient. He showed conspicuous emaciation and contractures of the lower extremities. Impression: suprasellar tumor. The patient was incontinent and became progressively worse.

Autopsy, March 22, 1922, showed an adenoma of the pineal gland with gliosis of the optic tracts.

Fig. 1 shows the results in Case I. The patient was incontinent, so that the urinary output could not be measured. The fluid intake, while not great, was distinctly increased for such a small boy. Without medication, the daily range was from 2200 to 3800 cc., whereas, when pituitary posterior lobe extract was given intramuscularly, the fluid intake ranged from 1100 to 2200 cc. When the extract was sprayed intranasally, he took only 900 to 2300 cc. of fluid, a result comparable to the effect of the drug intramuscularly.

CASE II.—J. E. L. (P.B.B.H., No. 33046, Surg. 16304) was a single woman, aged thirty-three years, who entered the hospital January 5, 1920, complaining of severe headaches, fifteen to twenty years in duration. In the preceding nine years she had experienced four severe attacks of headache lasting from four to fourteen days, accompanied by blurring of vision and diminution in hearing. During the attacks she experienced polyuria and drowsiness, but no nausea or vomiting. Physical examination showed suboccipital tenderness, slight neck rigidity, nystagmus to right and left, bilateral primary optic atrophy, bilateral hemianopsia, definite ataxia, and markedly hyperactive reflexes. Roentgen studies showed evidence of increased intracranial pressure and destruction of the sella turcica. On January 31, 1920, Dr. Cushing performed a right frontal osteoplastic exploration which disclosed a large cyst in the region of the optic chiasm. The cyst was evacuated and a piece of the cyst wall excised. Immediate examination of the fragment showed no evidence of malignancy. The patient made an uneventful recovery and was discharged four weeks later.

The severity and frequency of the headaches was definitely diminished but the patient developed polydipsia and polyuria of approximately 6 liters.

Fig. 2 shows the result of pituitary medication in this patient. The usual fluid intake without medication was between 5 and 7 liters. As may be seen from the figure, pituitary extract sprayed intranasally was quite as effective as intramuscular injection in checking the thirst and polyuria.

CASE III.—P. G. S. (P.B.B.H., No. 34591, Med. No. 19055) was a single woman, aged twenty-four years, who entered the hospital July 17, 1922, complaining of thirst and polyuria, thirteen years in duration. The family history and past history were not significant. Thirteen years before admission she first noticed increased thirst and urinary output. Physical exam-

ination and laboratory tests including Roentgen rays of the skull were negative. The spinal fluid was normal. There was no evidence of syphilis or tumor growth and a diagnosis of diabetes insipidus of unknown etiology was made. In 1923, during the eighth and ninth months of pregnancy, the symptoms spontaneously disappeared only to return immediately following parturition. When last heard from, approximately eighteen months after discharge from the hospital, the patient was still securing relief from intranasal pledgets of cotton.

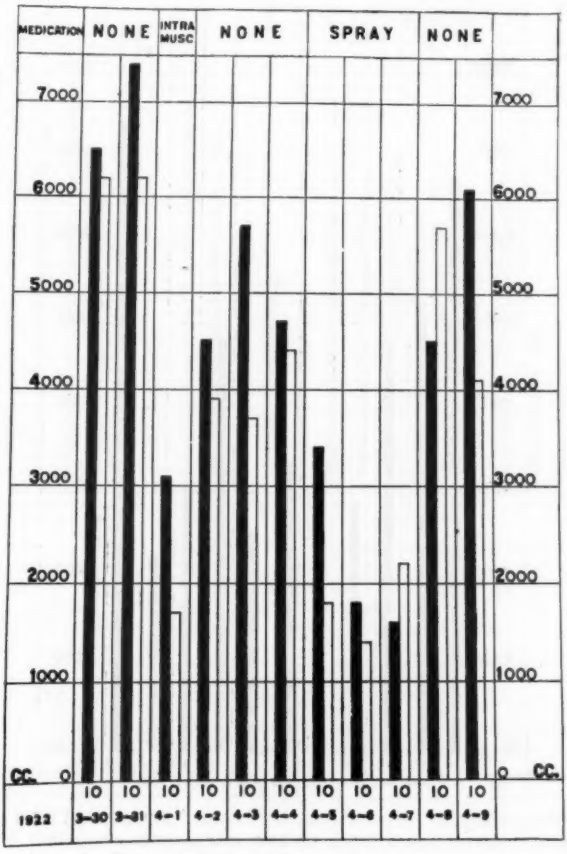

FIG. 2.—J. L., Surg. No. 16304 P.B.B.H. "I" denotes twenty-four hourly intake of fluids; "O" denotes twenty-four hourly output of urine; "Intramusc." 3/31/22, 1 cc. obstetrical pituitary extract (post. lobe) intramuscularly every six hours for 4 doses; "spray" 4/5, 4/6, 4/7, 1 cc. "obstetrical" pituitary extract every four hours.

Fig. 3 shows the effect of pituitary extract when given hypodermically and when given by spray. Both methods reduced the fluid intake and output to approximately one half their previous amounts. Again the effects of the two methods are practically the same.

CASE IV.—D. R. C. (B.C.H., No. 529901, T.M.L. 189) was a married woman, aged thirty-seven years, who entered the hospital complaining of polyuria and polydipsia four years in duration, and headaches and right tinnitus for one year. Her mother and younger sister had had tuberculosis. The present illness began five years before admission when, following a bad fall, she developed the signs and symptoms of pseudocyesis. She gained 50 pounds in weight, had amenorrhea, and her breasts became large and

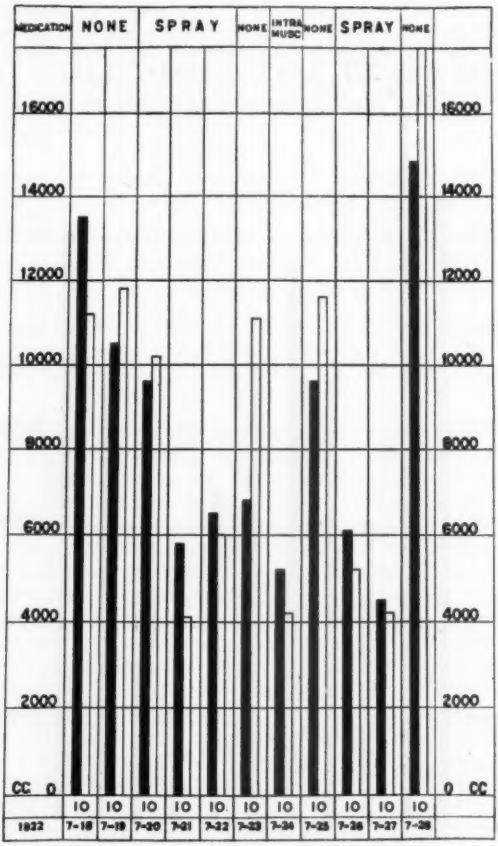

FIG. 3.—P. S., Med. No. 19044 P.B.B.H. "Spray" 7/20, 7/21, 7/22, 1 cc. "obstetrical" pituitary extract (post. lobe) sprayed intranasally every four hours. 7/24 1 cc. intramuscularly every six hours; 7/26, 7/27 "spray"—1 cc. sprayed intranasally every three hours.

secreted milk, but she was not pregnant. Polydipsia gradually developed following the pseudocyesis until, a year later, she drank from 25 to 30 glasses of water a day. One year before entry she noted almost constant buzzing in the right ear with weekly attacks of severe headache. One month before entry Dr. Cushing found the physical examination and special tests essentially negative and kindly referred the patient to us for further study of the effect of pituitary extract. The diagnosis was diabetes insipidus of unknown etiology.

Fig. 4 compares the results of the different methods of pituitary medication. Administration by swab was about as effective as hypodermic injections while the spray was somewhat less efficacious.

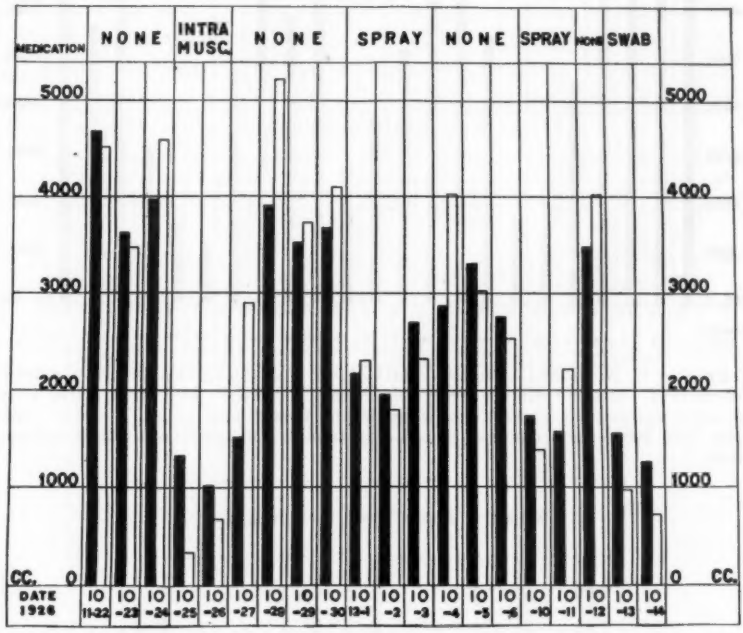

FIG. 4.—D. C., T.M.L., No. 189. "I" denotes twenty-four hourly intake of fluid, "O" signifies twenty-four hourly output of urine; 11/25, 11/26 "Intramusc." 1 cc. "obstetrical" pituitary extract intramuscularly every six hours. "Spray" 12/1, 12/2, 12/3, 1.5 cc. sprayed intranasally every six hours. "Swab" 12/13, 12/14, small pledget cotton soaked in 1 cc. pituitary extract (obstetrical) inserted into one side of nose every six hours.

CASE V.—H. N. (B.C.H. No. 531610, T.M.L. 199) was that of a single man, aged twenty-one years who entered the hospital complaining of polydipsia and polyuria of eighteen months duration. The past and family history was not significant except for an attack of influenza three years before entry. The present illness began eighteen months before admission when, without apparent cause, he noted the onset of increased thirst and urination. Physical examination and all special studies were negative.

The diagnosis was diabetes insipidus, possibly of postencephalitic etiology.

Fig. 5 shows the results in patient H. N. Pituitary extract by swab controlled the polydipsia and polyuria quite as effectively as when given hypodermically, while the spray was only slightly less effective.

CASE VI.—H. H. R. (B.C.H. 53732, T.M.L. 221) was a married woman, aged fifty-six years, who entered the hospital because of polydipsia and polyuria of eight months' duration. The family and past history was essen-

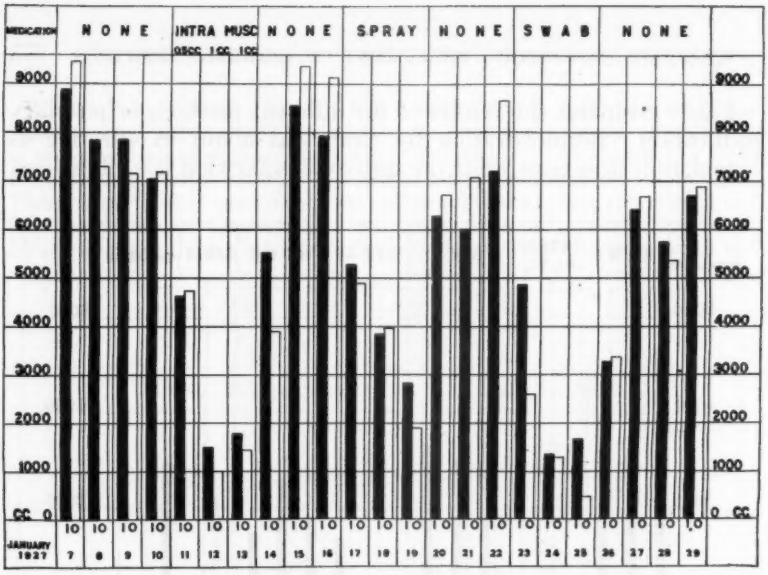

FIG. 5.—H. N., T.M.L. No. 199. 1/11, 1/12, 1/13, 0.5 to 1 cc. pituitary extract (obstetrical) intramuscularly every six hours. "Spray" 1/17, 1/18, 1/19, 1 cc. pituitary extract (obstetrical) five times in the twenty-four hours. "Swab" 1/23, 1/24, 1/25, nasal pack one side of nose, containing 1 cc. pituitary extract (obstetrical).

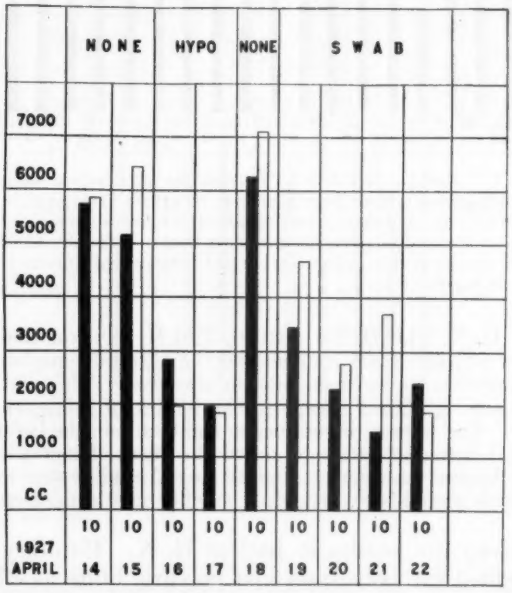

FIG. 6.—H. H. R., B.C.H. No. 53732, T.M.L. No. 221. 4/14 and 4/15, no medication; 4/16, 1 cc. (obstetrical) pituitrin at 8.00 A.M., 2.00 P.M. and 11.00 P.M. hypodermically; 4/17, 0.5 cc. of the drug hypodermically at the same hours; 4/19, 1 cc. on swab at 8.00 A.M., 5.00 P.M. and 11.00 P.M.; 4/20, 0.5 cc. on swab at 8.00 A.M., 12.00 M., 4.00 P.M. and 8.00 P.M.; 4/21, 0.5 cc. on swab at 8.00 A.M.; 2,00 P.M. and 11.00 P.M.; 4/22, 0.5 cc. on swab at 8.00 A.M., 12.00 M., 4.00 P.M. and 10.00 P.M. The last three days on the swab show a 2 liter intake and output with 2 cc. obstetrical pituitrin in twenty-four hours, or the same amount which was used hypodermically before entry. Since discharge, this patient has used only 1 cc. on the swab in twenty-four hours.

tially negative. Her illness began eight months before admission, when, without apparent cause, she noted the onset of increased thirst and urination. Physical examination and special laboratory tests were negative save for a slight defect at the upper outer angles of the visual fields. The diagnosis was diabetes insipidus, possibly due to brain tumor.

Fig. 6 shows the results of medication on the daily water intake and urinary output. The use of pituitary extract by nasal pledgets reduced the water intake and urine output to the level of normal quite as effectively as hypodermic administration.

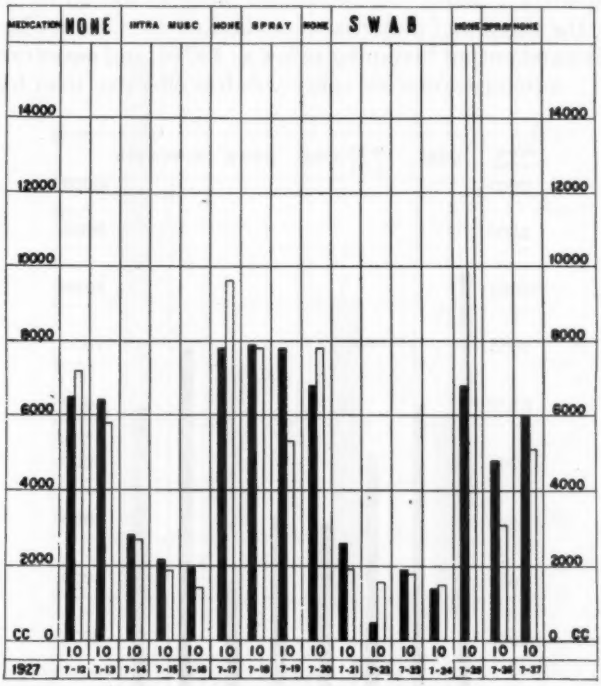

FIG. 7.—M. G., N.Y.H. No. 274076. 6/12, 6/13, no medication. 6/14, obstetrical pituitrin, 1 cc. every six hours; 6/15, 0.5 cc. every six hours; 6/16, every four hours; 6/17 no medication; 6/18, 1 cc. sprayed every six hours; 6/19 every four hours; 6/20, no medication; 6/21, 1 cc. obstetrical pituitrin on swab every six hours; 6/22, 0.5 cc. every six hours; 6/23, 6/24, 0.25 cc. every six hours; 6/25, no medication; 6/26, 1 cc. obstetrical pituitrin sprayed every four hours; 6/27, no medication.

CASE VII.—M. G. (N.Y.H. No. 274076)* was a single Italian laborer aged forty-five years, who entered the New York Hospital, July 6, 1927, complaining of excessive thirst and polyuria beginning five weeks previously. He had had a chancre six years before entry and had received several courses of intramuscular mercurial and intravenous arsenical treatments. Three years before entry his blood Wassermann test continued to be positive.

* The authorities of the New York Hospital have kindly permitted us to use the data secured in studying this patient.

Five weeks before entry he noted gradual increase of thirst and polyuria. He drank about 6 quarts of water daily. Physical examination was negative save for irregular pupils which did not react to accommodation. The blood Wassermann reaction was negative while the spinal-fluid reaction was positive. The fundi of the eyes were normal. The knee jerks were equal and hyperactive. The colloidal-gold curve was 2222221100. The diagnosis was diabetes insipidus due to central-nervous-system syphilis.

Fig. 7 shows that the fluid intake and urinary output ranged from 6 to 7 liters a day without medication, while pituitary extract hypodermically reduced the fluid intake and urinary output to approximately 2 liters. By intranasal pledgets soaked in pituitary extract, the thirst and polyuria were checked even more effectively, the intake and output becoming as low as 480 cc. and never exceeding 1900 cc. Administration by spray was less effective than by swab.

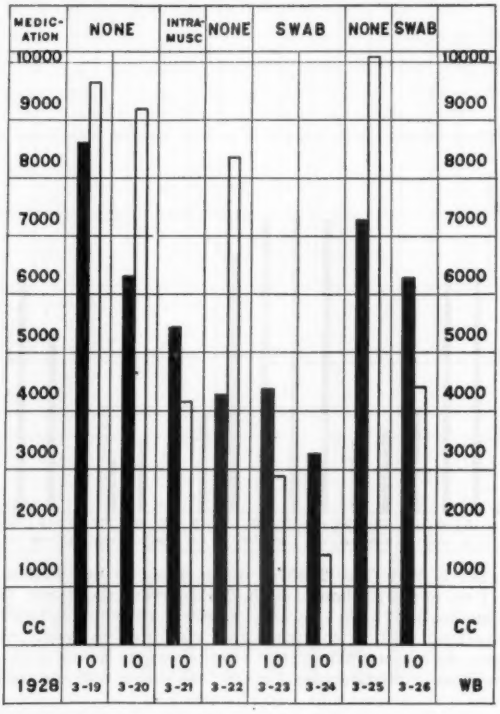

FIG. 8.—W. B., B.C.H. No. 558154. 3/19, 3/20, no medication; 3/21, 1 cc. obstetrical pituitrin, hypodermically, every six hours; 3/22, no medication; 3/23, 3/24, 1 cc. obstetrical pituitrin on swab every six hours; 3/25, no medication; 3/26, 0.5 cc. surgical pituitrin every six hours on swab.

CASE VIII.—W. B. (B.C.H. No. 558154) was a married woman, aged forty years, who entered the hospital complaining of frequent urination, thirst, headaches, and vomiting, eight months in duration. The family history, marital, and past histories were essentially negative. Her illness

began eight months before entry, when she noted polyuria followed, a month later, by polydipsia. Three months before entry she first experienced dull frontal headaches which, one month before entry, became associated with nausea and vomiting. Physical examination showed all reflexes hyperactive, especially on the left side. Roentgen ray studies of the skull showed evidence of increased intracranial pressure. Study of the visual fields showed a right temporal hemianopsia. Physical examination and special tests were otherwise negative. The diagnosis was diabetes insipidus, probably due to brain tumor.

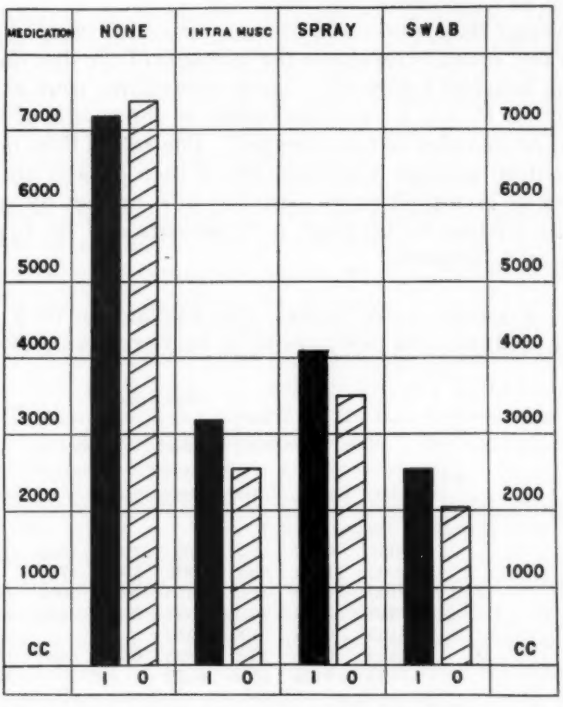

FIG. 9.—Averages of the effect of pituitary posterior lobe on the fluid intake and urinary output compared to the effect on days on which no medication was given. "I" indicates fluid intake, "O" urinary output, "Intramusc." indicates hypodermic injection, "spray," nasal spray and "swab," pituitary extract given by pledgets of cotton. The average fluid intake and urinary output indicates the average of 7 of the 8 patients; Patient I being excluded because of incontinence. The fluid intake and urinary output during the first one or two days of the patients' stay in hospital were used in obtaining the average figures for the group. The effect of giving pituitary extract by spray was studied in 6 patients; by swab, in 5 patients, and by hypodermic injection in 8 patients.

The results of treatment shown in Fig. 8, while not so striking as those observed in the other cases, conform in general to the effects observed in the preceding 7 patients. The effects of application of pituitary extract by intranasal pledgets (swab) are about as marked as when hypodermic injections were given. The reduction of

intake is especially striking. It is interesting to note that on March 22 when no medication was given, the intake remained low while the urinary output rose considerably. A somewhat similar phenomenon occurred on March 25.

In all of the 8 patients studied, the urine was of low specific gravity and contained no sugar, albumin, casts or other abnormal elements. In each of the preceding 8 patients studied, intranasal application of posterior lobe pituitary extract was as successful in controlling the symptoms as hypodermic injection.

The average fluid intake and urinary output are charted in Fig. 9. The first two columns represent the averages of the first days of the patient in hospital before the various procedures were attempted.

Patient M. P. No. 1 was incontinent, so the results of his study could not be included in the averages. The actual fluid intake and urinary output average measurements of each patient are given in The effect of giving pituitary posterior lobe extract by spray was studied in 6 patients; by swab in 5 patients and by hypodermic injection, in 8 patients.

TABLE I.—AVERAGE FLUID INTAKE AND URINARY OUTPUT IN CUBIC CENTIMETERS IN PATIENTS WITH DIABETES INSIPIDUS.

	Medication.							
	None.		Intramuscular.		Spray.		Swab.	
	Intake.	Output.	Intake.	Output.	Intake.	Output.	Intake.	Output.
Patient 1	6950	6200	3100	1700	2267	1800		
Patient 3	12000	11500	5200	4200	5300	4700		
Patient 4	4100	4200	1215	510	2028	2004	1405	845
Patient 5	7910	7783	2633	2393	3980	3593	2627	1453
Patient 6	5465	6135	2400	1910	....	....	2405	3255
Patient 7	6450	6500	2300	1993	6833	5400	1595	1688
Patient 8	7455	9425	5416	4150	....	....	4632	2927
Average . . .	7190	7392	3181	2408	4082	3499	2533	2034

Discussion. The effect of pituitary extract in controlling the symptoms of polyuria in the patients studied was prompt and conspicuous in all instances. Practically all patients lost the "cottony" feeling in the mouth and throat and noted a more abundant flow of saliva. Several remarked that they perspired for the first time in months. Instead of dry skin and chapped lips being present, the skin and mucous membranes assumed more normal characteristics. Coincident with pituitary medication the patients usually gained in body weight and showed by the relative decrease in urinary output, a retention of water within the body. Usually the day following

withdrawal of pituitary extract the urinary output was relatively excessive and the body weight decreased in several instances as much as 3 or 4 pounds. Whether this retention of water was mainly in the blood or tissues cannot be stated on the basis of the available facts although the above clinical observations and the appearance of pitting edema in 2 patients would point to considerable retention of water in the tissues. Water retention was evident in patient No. 2 on the first day that pituitrin was given by intranasal spray, April 5, 1922; while on April 8, 1922, the first day after pituitrin was withdrawn, the urinary output exceeded the water intake by over a liter. The same preponderance of urinary output is shown strikingly in patient No. 3 on July 23, July 25 and July 28, 1922. Examination of the other figures shows similar changes in all of the patients.

The intranasal use of pledgets of cotton soaked in posterior lobe pituitary extract not only controlled the polydipsia and polyuria of the patients while in the hospital, but was equally effective when the individuals themselves continued treatment. Patient 2, for instance, was able to commence active work. Patient 3 when last heard from eighteen months after discharge from the hospital was still securing relief from intranasal applications. Patient 4 was able to return to a normal social life and make extensive trips which formerly would have been impossible. Patient 5 has been able to return to work and support himself for the last eighteen months, and Patient 6 has likewise experienced relief from continued use of intranasal pledgets, soaked with pituitary extract. In no instance has there been any evidence of decreased benefit from continued use. Probably the result most gratifying to all patients has been the enjoyment of uninterrupted sleep.

It is somewhat surprising that the intranasal application should be so strikingly effective for, although a cubic centimeter of pituitary extract is used in soaking the pledget of cotton, by far the major part is again withdrawn on removing the pledget after six hours. The conspicuous effect of such relatively small amounts must be due to the continuous intranasal absorption over a long period of time.

The effect of a single subcutaneous dose of pituitary extract is evident for only three or four hours.[3] That only a very little of the drug is needed at a time is shown by the fact that a very definite diminution in urinary output may be caused by only 0.004 cc. pituitary extract hypodermically (Patient H. N.).

The absorption of pituitary extract intranasally is of considerable physiologic interest because of the failure of benefit when given by mouth, in salol-coated tablets, by duodenal tube, or when administered by vagina or rectum. As has been pointed out in previous communications,[4, 5] the peculiar physiologic absorptive property is related to the unusual anatomic structure of the nasopharynx in possessing free nerve endings that penetrate through the mucous membrane. As shown in animals, crystalloids, colloids, and to a

lesser extent even particulate matter traverse the nasopharyngeal mucous membrane by being absorbed by way of the lymphatics of the olfactory nerve cells and thence to the systemic lymphatics. In several patients we have secured corroboratory evidence of lymphatic absorption by applying adrenalin before pituitary posterior lobe extract. If absorption were by vascular routes one would expect lessened evidence of pituitary absorption under such circumstances. The previous application of adrenalin seemed to have no influence on pituitary absorption, a result in harmony with the previous observations.

Since the area of active absorption is limited to the olfactory area at the roof of the nasopharynx, it is absolutely essential to place the pledget of cotton soaked in pituitary extract high in the nasopharynx. Failure to observe this precaution may well explain the somewhat irregular results observed by others.

Summary and Conclusions. 1. Eight successively observed cases of diabetes insipidus of various etiologies have been studied.

2. Intranasal application of posterior lobe pituitary extract was as efficacious as hypodermic injection in controlling the fluid intake and urinary output.

3. Attention is drawn to the importance of inserting the cotton pledget soaked with pituitary extract high in the nasopharynx.

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AN ELECTROCARDIOGRAPHIC STUDY ON 123 CASES OF DIABETES MELLITUS.*

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In the early days of insulin therapy it was observed that in cases of diabetes mellitus with cardiovascular disease the symptoms of

* Presented at the Annual Meeting of the Association of American Physicians, Washington, D. C., May, 1928.

the latter condition often persisted, and in some instances progressed causing death despite the successful treatment of the diabetes. This was rather a disappointment for it was hoped that the reëstablishment of a normal metabolism would eventually have a favorable influence on the course of the coëxisting cardiovascular disease. The control of diabetes mellitus, made possible by the discovery of insulin, provided conditions for a more satisfactory study of the effects produced by the abnormal metabolism present in this disease on other tissues in the body, particularly the myocardium and vascular system. In an attempt to ascertain the effects of the diabetes mellitus on the myocardium, it was decided to have an electrocardiogram taken on all diabetic patients before treatment was instituted and after the diabetic condition had been controlled by diet or diet and insulin.

Since the beginning of 1925, electrocardiograms have been made on diabetic patients before and at intervals after the beginning of treatment with the view of determining: (1) The proportion of cases having significant electrocardiographic abnormalities; (2) if any changes present in the electrocardiograms were characteristic of diabetes mellitus; (3) if control of the diabetes by diet with or without insulin resulted in electrocardiographic improvement.

In this study, premature beats, high *T* or *P* waves, negative *T* wave in Lead III, and left ventricular preponderance were included among the normal electrocardiograms. A number of cases were excluded from this series for the following reasons: (1) When digitalis had been used during the eight weeks prior to taking the electrocardiograms; (2) when hyperthyroidism was present with diabetes mellitus; (3) when, in cases originally diagnosed diabetes mellitus, the glycosuria disappeared and the glucose-tolerance test returned to normal after the removal of foci of infection. (These cases, by the way, all showed normal electrocardiograms.)

All patients received the regular treatment prescribed in this clinic for diabetes mellitus.[1] The discharge diet contained calories 40 to 50 per cent above the basal requirement, protein, 0.6 to 1 gm. per kilo body weight, and a fatty acid-total glucose molecular ratio of about 1.3 to 1. In cases not controlled by diet, an adequate amount of insulin was given to maintain the urine free from sugar and the fasting blood sugar not exceeding 0.13 per cent or, at the most, 0.16 per cent in elderly patients.

In the clinical survey the age of the patient, duration of diabetes and its severity, as evidenced by the need for and amount of insulin, were noted. Blood-pressure readings were taken and the diagnosis of peripheral arteriosclerosis was based only on the presence of unquestionable thickening and tortuosity of the peripheral arteries. Signs of cardiac failure and evidence of heart disease from any cause were looked for. After the patients left the hospital, an attempt was made to determine the strictness of their adherence to treatment,

their present state of health if alive and the cause of death in fatal cases.

Of the 123 cases in this series 56 (45.5 per cent) showed significant electrocardiographic changes of which negative *T* waves in Leads

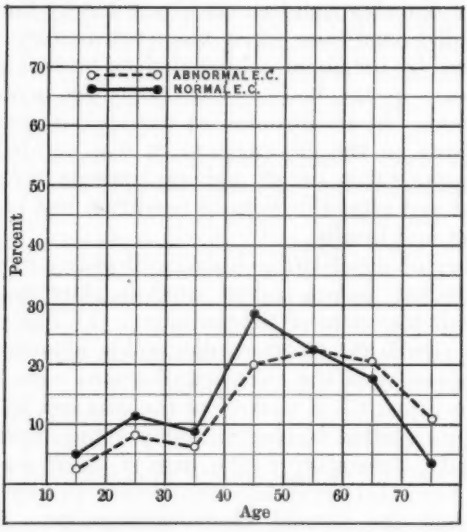

CHART I.—This chart shows the age grouping of the patients studied.

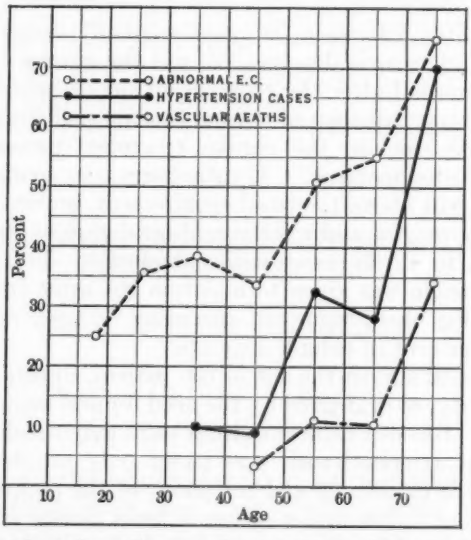

CHART II.—This chart shows the percentage of abnormal electrocardiograms, cases of hypertension and vascular deaths according to age groups.

II and III were the most common. There were several cases of auricular fibrillation, negative T_1, and negative T_1, $_{II}$ and $_{III}$, right branch bundle block, low voltage, and 1 case of prolonged P–R interval.

TABLE I.—COMPARISON OF CASES WITH NORMAL AND ABNORMAL ELECTROCARDIOGRAMS.

	Normal, per cent.	Abnormal, per cent.
Under 40 years of age	27.0	18.0
Hypertension	15.0	31.0
Cardiac failure	1.5*	18.0
Arteriosclerosis	13.0	34.0
Diabetes—less than 1 year	33.0	48.0
Diabetes—1 to 6 years	52.0	45.0
Diabetes—over 6 years	15.0	7.0
No insulin	22.0	41.0
Over 40 units insulin daily	34.0	27.0
Mortality	4.4	26.7

* One case, an obese diabetic without hypertension, suffering from swelling of the feet, the only sign or symptom present suggesting cardiac failure.

Group with Abnormal Electrocardiograms. Fifty-four of the 56 cases with abnormal electrocardiograms have been traced and of these 15 are dead. Ten cases died of vascular disease: 7 cardiac, 1 hypertension and intestinal hemorrhage, 1 hypertension and cerebral hemorrhage, 1 hypertension and chronic nephritis with calculi and pyelitis. Of the 7 cardiac deaths, 6 showed signs of cardiac failure at the onset of diabetic treatment and all died within one year with the exception of 1 case dying in sixteen months. The seventh cardiac death occurred in a patient with peripheral arteriosclerosis but no signs of cardiac failure at the beginning of treatment. The electrocardiogram in this case showed low voltage and auricular premature beats and death took place within two months of the beginning of treatment. In all the patients dying of vascular disease the diabetic condition was under control by diet or diet and insulin. Of the other 5 fatal cases, 2 died in coma (neither adhered to diet at all after leaving hospital), 1 of acute pyelonephritis, 1 of lobar pneumonia and the other had hemochromatosis and may have died of cardiac failure. The ages of the 15 who died were all over forty-five years, except one of the coma cases who was twenty-seven years. There were 7 cases of peripheral arteriosclerosis, 6 cases of hypertension, and 6 cases of cardiac failure among those who died. The ages were greater, as was the incidence of arteriosclerosis, hypertension and cardiac failure, than in any of the other groups.

Twenty-three cases returned for one or more electrocardiograms after leaving hospital. In most instances, the final check was made from eight to twelve months after the beginning of diabetic treatment. In 15 cases the electrocardiogram had returned to normal, in 6 it was unchanged, and in 2 it showed more serious abnormalities.

Of the 15 whose electrocardiograms became normal it was seen that the abnormalities which disappeared were negative T waves in Leads II and III (7 cases), low voltage, negative T_1, auricular fibrillation, and 1 case of Q–R–S. aberration. The ages varied from twenty-seven to seventy-two, with 4 cases under forty-five years, and the average severity and duration of the diabetes were much the same as for the series as a whole. A clinical diagnosis of peripheral arteriosclerosis was made in 4 of the 15 cases. One noteworthy point is that this group included no cases of hypertension or cardiac failure. Of the 2 cases showing more serious electrocardiographic abnormalities, 1 patient with hypertension had not adhered to diet, and the other was a very severe case of diabetes of short duration.

Sixteen other cases with abnormal electrocardiograms are known to be alive and following treatment but did not return for reëxamination from considerations of distance and finances. Two are suffering from hemiplegia, 1 from cardiac failure, 1 is in a sanitarium with pulmonary tuberculosis, and the remainder are apparently well.

An analysis of this group with abnormal electrocardiograms would appear to show: (1) That in cases of diabetes mellitus suffering from vascular disease with signs of cardiac failure at the beginning of diabetic treatment, the cardiac failure progresses despite the control of the diabetes mellitus; (2) that in diabetes mellitus cases without hypertension and showing no signs of cardiac failure at the beginning of treatment, the abnormal electrocardiogram returns to normal in a fair percentage of cases following effective treatment of the diabetes mellitus.

TABLE II.—GROUP WITH ORIGINALLY ABNORMAL ELECTROCARDIOGRAMS.

	Cases.	Hypertension.	Cardiac failure.	Arteriosclerosis.
Dead	15	6	6	7
Normal	15	0	0	4
Unchanged	6	1	0	0
More abnormal	2	1	0	1
Unchecked cases	16	8	2	5
Untraced cases	2	1	2	2
	56	17	10	19

Group with Normal Electrocardiograms. Sixty-seven cases had normal electrocardiograms at the beginning of treatment. None of the cases in this group showed signs or symptoms of cardiac failure with the possible exception of 1 case, an obese diabetic with swelling of the feet. Eleven had hypertension. At present 2 cases have been lost sight of, 62 are living and 3 are dead. Chronic nephritis, peritonitis and pulmonary tuberculosis each accounted for 1 of the deaths. The fatal cases of nephritis and peritonitis both died within two months of the institution of diabetic treatment and it is

interesting to note that both had hypertension and 1, the chronic nephritic, had in addition gangrene with infection, yet each showed a normal electrocardiogram. In this group with normal electrocardiograms, there were no deaths from diabetes mellitus and only 1 from vascular disease, the case with chronic nephritis and hypertension.

Thirty-two cases returned for a recheck and in only 1 case was the electrocardiogram found to be abnormal. This was a patient with severe diabetes requiring 60 units of insulin daily who did not adhere to treatment after leaving hospital. Among the 31 cases with electrocardiograms remaining normal there were 4 originally having left ventricular preponderance who, on recheck, showed no preponderance, and 1 case with no preponderance at the time of first examination showed left preponderance on later examination.

TABLE III.—GROUP WITH ORIGINALLY NORMAL ELECTROCARDIOGRAMS.

	Cases.	Hypertension.	Cardiac failure.	Arteriosclerosis.
Dead	3	2	0	1
Normal	31	5	0	4
Abnormal	1	0	0	0
Unchecked cases	30	4	1*	4
Untraced cases	2	0	0	0
	67	11	1	9

* This is the same case that was noted in Table I.

Comment. Although the series of cases studied is not very large and the period of observation rather short, the findings appear to be of sufficient interest to report at this stage of the investigation. It has been shown that in a series of 123 diabetic patients 56 showed serious electrocardiographic abnormalities at the beginning of diabetic treatment and that in a very fair percentage the electrocardiograms returned to normal after the diabetic condition was controlled by treatment. It would appear from these observations that in the cases in which the electrocardiograms returned to normal after the diabetic condition had been controlled that the abnormal electrocardiograms had resulted from the effect on the myocardium of the perverted metabolism present in diabetes mellitus. Whether this is a direct action on the myocardium or an indirect one resulting from disease of the coronary arteries, or both, is difficult to answer. If one considers first the possibility of a direct effect on the myocardium, it may be stated that none of the few cases of severe acidosis studied showed an abnormal electrocardiogram and that many severe diabetics with hyperglycemia had normal electrocardiograms. As hyperglycemia and the products of the perverted metabolism present in diabetes mellitus apparently do not produce a direct effect on the myocardium resulting in an abnormal electrocardiogram, the possi-

bility of an indirect effect from disease of the coronary arteries appears more likely. In support of this view, it is known that similar types of electrocardiograms are found in nondiabetic patients suffering from cardiovascular disease and are supposed to result from the indirect effect produced on the myocardium from disease of the coronary arteries. In diabetic patients with symptoms of cardiovascular disease and having abnormal electrocardiograms, it has been shown that the control of the diabetic condition does not result in a cure of the cardiovascular symptoms or cause a return of the electrocardiogram to normal. Further, the presence or absence of diabetes mellitus in patients dying of cardiovascular disease does not alter essentially the clinical or pathologic findings with reference to the cardiovascular system. It seems fair to conclude then that the abnormal electrocardiograms present in this series of cases of diabetes mellitus have resulted from the effects on the myocardium of disease of the coronary arteries. If this be true, it is reasonable to assume that the same cause or causes are responsible for disease in other arteries of the body. As the chief cause of death in diabetes mellitus is vascular disease, its prevention in the young diabetic and an attempt to control further development in the older diabetic are of extreme importance.

In a discussion on the relationship of arteriosclerosis to diabetes mellitus, Joslin[2] has clearly shown the effects of present methods of treatment of diabetes mellitus on the clinical course of this disease and has stressed the importance of the prevention and control of vascular disease in diabetes mellitus. In considering factors responsible for the development of vascular disease at an early age in diabetes mellitus, he has suggested the high percentage of fat in the diabetic diet as a cause. It is not our intention at this time to enter into a discussion on this suggestion except to raise the question: Is the fat in the diabetic diet or the presence of diabetes mellitus the chief factor responsible for the development of vascular changes? In the series of cases reported here all patients received diets concontaining the same percentage of fat. Of 67 with normal electrocardiograms at the beginning of treatment 31 of 32 cases reëxamined have remained normal for periods varying from six months to over a year. The only case showing an abnormal electrocardiogram later was a patient who had not adhered to diet. In the group of 56 with abnormal electrocardiograms originally, 23 cases returned for reëxamination and in 15 the electrocardiogram was found to have returned to normal. The period of observation in this series is too brief to draw any definite conclusion as to the rôle of the fat in the diet in affecting the coronary arteries. The results, however, show that with the diet prescribed the normal electrocardiogram remains normal and the abnormal tends to improve.

If one considers the vascular changes leading to death in diabetes, it is found that they are chiefly, if not wholly, confined to the intimal

coat of the vessel, whether it be in the arteries of the heart, brain, kidney or lower extremity.[3] Further, the early intimal changes are inflammatory in type, degenerative changes being secondary and appearing later. It is generally believed that no single factor is responsible for these changes in the intima. Yet there is general agreement that infection is the most important single cause.[3,4] The improvement in the symptoms of patients with cardiovascular disease following the removal of foci of infection, so striking in some with angina pectoris, is a clinical indication of the causal relationship of infection to disease of the coronary arteries and suggests that the condition of the vessel improves after the removal of infection. May this not occur in diabetes mellitus? The susceptibility of diabetic patients to infection and the detrimental effects of infection on the clinical course of diabetes mellitus, particularly in untreated diabetics, are only too well known. Is it not probable that in diabetes mellitus the premature development of vascular changes is the result of infection acting in the presence of the abnormal metabolism of diabetes mellitus? If this be the case, one's efforts ought to be directed to prevention and eradication of infection as well as to restoration of a normal metabolism.

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NEUROGENIC DISORDERS OF THE HEART.*

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The symptoms that, to the laity and to most physicians, indicate heart disease, in reality are determined not by a disordered structure and mechanism of the heart itself, but rather by an insufficiency of the circulation. The primary function of the circulation is to maintain a volume flow of blood adequate for the metabolic needs of the tissues. The blood is the vehicle for the transport of gases, food elements and catabolites to and from the tissues, and it is in the capillaries that the metabolic exchange, the vital function of the circulation, is achieved. Symptoms of circulatory insufficiency arise when there is widespread impairment of the bloodflow through

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the capillaries. Many elements are concerned with the maintenance of an adequate circulation, among the most important of which are: (1) The heart, depending largely on its rate and rhythm, on the functional efficiency of the myocardium, and the intactness of the several valves; (2) the elasticity of the aorta; (3) the tone of the arterioles, capillaries and venules; (4) the arterial blood volume; (5) the blood viscosity; (6) the concentration of hemoglobin in the blood; (7) the ventilating capacity of the lungs; (8) the action of the striated muscles as a peripheral pump; (9) the proper functioning of the afferent and efferent nervous pathways to the heart and bloodvessels.

These factors are all so closely interlinked, and compensatory adjustments between them occur so speedily and automatically that it is most difficult in any particular case of circulatory insufficiency to determine the factor or factors at fault. Most difficult of all is the recognition of general circulatory disorders caused by disturbances in the nervous mechanism of the heart and bloodvessels. These neurogenic disorders are still very obscure because of the inadequacy of our knowledge of the control of the heart by its extrinsic nervous apparatus. An analysis of the available experimental and clinical facts is of value for the sake of orientation and for the planning of future studies.

A brief review of anatomy and physiology will clarify the discussion.[1] The heart is supplied with both afferent and efferent fibers. It is hardly necessary to give a detailed description of their course. The vagus inhibitory fibers arise in the dorsal vagus nucleus and leave the main trunk of the vagus in three branches, one arising just below the superior laryngeal, one at the level of the inferior laryngeal nerve, and one in the thoracic portion of the vagus. They intermingle with branches of the sympathetic to form the superficial and deep cardiac plexuses. The vagal fibers end around ganglion cells in the heart. The right vagus, after traversing the deep cardiac plexus between the aorta and pulmonary veins, inosculates in the regions of the auricular septum, the sinoauricular node, and the auriculoventricular node; the left vagus shares in the formation of the superficial cardiac plexus between the aorta and pulmonary artery and passes to the heart along the left coronary artery reaching both nodes.

The fibers of the sympathetic or accelerator nerves arise from cells in the lateral horns in the last cervical and upper dorsal spinal segments, and, leaving the cord through the anterior roots, form part of the spinal nerves and then pass to the superior, middle and lower cervical ganglia through the white rami communicantes, where they end around ganglion cells. From the superior and middle cervical ganglia, as well as from the stellate ganglion, which consists of the inferior cervical and upper thoracic ganglia, postganglionic fibers pass as the three cardiac nerves which enter the

superficial and the deep cardiac plexuses and so pass to the heart. The right vagus and sympathetic affect in particular the pacemaker of the heart, the sinoauricular node, the left vagus and sympathetic seem to have a predominant influence on the auriculoventricular node.[2] Nothing is known about the intracardiac nerves, whether they belong to the vagus or the sympathetic system. Motor end plates have been described on these nerves.

The best known of the afferent pathways is the depressor nerve,[3] arising from the root of the aorta and passing upward from here as a more or less well-defined nerve filament to join the vagus at about the level of the superior laryngeal nerve, and so reaching the medulla. Stimulation of the depressor nerve causes a reflex lowering of the blood pressure and a slowing in pulse rate.

It is certain that other centripetal pathways exist, but their course is unknown. Central stimulation of the superficial nerves of the ventricles may cause slowing or acceleration of the heart beat.[4] Some of these afferent fibers probably pass through the vagus. The afferent pathway through the sympathetic—which has received so much attention in recent years in connection with operations for the relief of angina pectoris—passes through the middle and inferior cardiac nerves to the middle cervical and stellate ganglia, and reaches the central nervous system through the rami communicantes of the lower cervical and upper six thoracic spinal segments, coming in close relationship with the cerebrospinal system in the posterior-root ganglia. These afferent fibers do not conduct sensations of pain or of touch. This was known to Harvey, who had the opportunity of examining a man who had lost part of his thoracic wall. Harvey wrote . . . "the heart was without the sense of touch, for the youth never knew when we touched his heart, except by the sight or the sensation he had through the external integument."[5] Other observers have confirmed this fact.[6] Singer[7] has pointed out that experimentally, injury of the adventitia of the aorta or coronary arteries produces pain, but that the heart itself is insensitive. Finally, Hatcher and Weiss[8] have shown that the vomiting in digitalis intoxication is dependent on the integrity of afferent pathways from the heart and suggest that the nausea, vomiting and belching, that so commonly accompany coronary occlusion and angina pectoris are reflexes through the same nervous pathways.

Efferent impulses over the vagus not alone slow the heart rate, they diminish the magnitude of contraction of the auricles, and to a less extent of the ventricles, they retard conduction of the cardiac impulse, and reduce the irritability of the heart muscle. Efferent impulses over the sympathetic nerves accelerate the heart rate, increase the magnitude of contraction of auricles and ventricles, and augment the speed of conduction. Both nervous pathways are constantly in a state of excitation, yet they do not act altogether as

true antagonists. The heart rate and rhythm depend in large part on variations in the degree of excitation of these two sets of nerves. These variations are determined by reflexes passing over innumerable afferent pathways. This regulation of the activity of the heart is an adaptive mechanism enabling the heart to meet the demands placed on it by the varying activities of the body. Loss of this regulatory function may have serious consequences. Complete denervation of the heart, that is, severance of all of the extrinsic cardiac nerves, greatly restricts the activities of an animal. In dogs who have survived this operation for many months, the circulation is adequate when they are at rest, but any greater physical exertion is impossible. The animals collapse from exhaustion and there is no acceleration of the heart.[9]

The afferent arcs of the cardiac reflexes may arise in almost any part of the body. They may come from the heart itself, from the lungs, and other viscera, they may pass through the segmental parts of the nervous system, that is, the cranial nerves, or the spinal nerves. Afferent impulses may also reach the vagus and sympathetic nuclei from all suprasegmental parts of the brain. One need but recall the changes in heart rate accompanying emotions and varying psychic states. No convincing proof has been offered of the existence of cardiac reflex arcs to the hypothalamus and I believe with François-Franck and with Tigerstedt that the vital cardiac reflex arc passes through the medulla and that the brain acts as a peripheral organ initiating reflexes *via* the medulla. Centripetal stimuli passing through the vagus and trigeminus seem always reflexly to slow the heart. Activity of the other centripetal nerves may give rise to retardation or acceleration. Weaker stimuli seem to increase the heart rate, stronger ones to decrease it. Reflex slowing of the heart is determined largely by increased activity of the vagus center, to a less extent by a diminished tonus in the accelerator centers. Reflex acceleration of the heart is due to lessened vagus tonus and increased tonus of the accelerator centers.

The tonicity, that is, the constant activity of the cardiac centers, is determined in part by the steady inflow of afferent impulses, but also, in case of the vagus nucleus, at any rate, by the oxygen and carbon dioxid content, as well as the hydrogen-ion concentration of the blood.

At first blush it would seem simple to classify and describe, on the basis of the anatomic and physiologic data, the various cardiovascular syndromes that must arise with disturbances of innervation of the heart. In actual fact such a study is of limited value, for cardiac disorders due to focal lesions involving the heart nerves or nuclei are quite rare. The following classification may, however, be attempted. Its value lies chiefly in its demonstration of the limitations of our knowledge.

A Classification of Neurogenic Disorders of the Heart.

A. I. Disorders of the nervous structures in the end organs.
   1. Vagus.
   2. Sympathetic.
   II. Disorders of the ganglionic arc.
   1. Vagus.
   2. Sympathetic.
   III. Disorders of the segmental arc.
   1. Vagus.
   (*a*) Nerve trunk.
   (*b*) Dorsal nucleus.
   2. Sympathetic.
   IV. Disorders of the hypothalamic arc.
   1. Vagus.
   2. Sympathetic.

B. Disorders due to excessive or exaggerated afferent stimuli.
   1. Segmental.
   (*a*) Somatic.
   (*b*) Visceral.
   2. Suprasegmental.
   Cerebral (abnormal mental states).

C. Disorders due to increased irritability of the visceral nervous system of unknown localization.
   1. Constitutional.
   2. Acquired.
   (*a*) Infectious.
   (*b*) Internal secretory.

D. Disorders secondary to neurogenic vasomotor disorders.

Let us discuss the known neurogenic cardiovascular syndromes in the light of this classification. I know of no cardiac disturbances that may be placed in Groups I and II, although Leriche's[10] observations made on patients undergoing sympathectomy under local anesthesia, that electrical or mechanical stimulation of the left stellate ganglion could cause attacks of angina pectoris, suggest that lesions of the stellate ganglion, were they to occur, might cause this syndrome.

Group III, disorders of the segmental arc, is represented in medical periodical literature by innumerable inconclusive case reports. Forty and fifty years ago when physiologists were devoting much of their attention to the cardiac nerves, clinicians began reporting cases of tachycardia due to vagus injury. Martius[11] could find only 24 among these with autopsy control. Yet even in this selected group there is hardly one which will stand critical analysis. Among the conditions which were supposed to lead to vagus tachycardia were compression of the vagus by mediastinal tumors, tuberculous

lymph nodes, aortic aneurysms, alcoholic neuritis of the vagus, and destruction of the dorsal vagus nucleus in bulbar palsy. Yet, in practically every case there existed in addition to the nerve lesion other potent causes of tachycardia such as fever, dyspnea, toxemia or anxiety. Possibly 2 cases of tachycardia accompanying bulbar palsy described by Charcot[12] and by Duchenne[13] may be accepted as legitimate. On the other hand, neurogenous forms of Stokes-Adams' syndrome have been described. In very few of them, however, has unequivocal evidence of the intactness of the conducting system of the heart, associated with a lesion of the vagus been offered. Kahler[14] described a patient suffering from cerebrospinal syphilis, who had attacks of loss of consciousness followed by arrest of the heart action. Electrocardiograms taken during the attack showed no auriculoventricular dissociation. The pulse rate between the attacks was about 80. The patient died during a seizure. Necropsy revealed no evidence of disease of the conducting system, but degeneration in the dorsomedial nucleus of the vagus. A somewhat similar picture has been described in a patient with epidemic encephalitis, but without anatomic verification.[15]

Just as in a previous generation it was the fashion to ascribe certain cardiac disorders to lesions of the vagus, or even to vagus neuroses, so in our day there seems to be a tendency to invoke lesions of the visceral part of the hypothalamus in explanation of certain cardiac and vasomotor disorders accompanying encephalitis and other disease processes that involve this portion of the brain. To my mind there is little, if any, justification for this hypothesis. First, although much evidence has been presented that disturbances of certain vegetative functions may be associated with lesions in the floor of the third ventricle,[16] no physiologic or anatomic proof has been offered that the heart is controlled from this region. Indeed the literature on encephalitis contains few references to this matter. It may be worth while to dwell for a moment on the pulse rate in this disease, for its study well illustrates the difficulties involved in most attempts to estimate the significance of abnormal heart rates. During the febrile stage of epidemic encephalitis, as in most febrile states, the pulse rate is elevated in proportion to the fever. This is due to general causes. With the subsidence of the fever, the heart rate returns to normal figures. In the late postencephalitic stages, when tremor and rigidity have set in, the heart rate again tends to be accelerated. But now the increased rate is determined by the muscular exertion incident to the tremor and rigidity, not by central factors. In order to test this interpretation, I have measured the pulse rate in 8 patients with the postencephalitic Parkinsonian syndrome, first while awake and at rest in bed, and again during sleep, noting in particular the degree of tremor and rigidity on each occasion. With the exception of one man with marked rigidity, whose pulse rate ranged between 44 and 60, all of the rates were

between 66 and 106. The more rapid pulse rates were found in patients with more marked muscular disturbances. During sleep these rates were reduced roughly in proportion to the degree of muscular relaxation that ensued. Thus a man with considerable rigidity and tremor had a waking pulse rate of 92; during sleep, in which there was marked relaxation, the pulse rate was 66. Similar readings in another patient were 102 and 72. Such observations illustrate the great caution that must be employed in interpreting abnormal heart rates.

It is apparent that focal lesions of the extrinsic nervous apparatus of the heart play no significant rôle in the genesis of cardiac disorders. Neurogenic circulatory disturbances fall chiefly within the last three categories of our classification. The first group comprises cardiac disorders due to excessive or exaggerated afferent stimuli. The tachycardias accompanying states of muscular tremor and rigidity may be ascribed to centripetal impulses initiated by muscular activity. They are of little clinical importance. Of more significance are reflexes initiated by visceral disorders. Here may be grouped the simple tachycardias, and occasional bradycardias associated with disease of the gall bladder, stomach, and other internal organs. Of greater import, however, are the occasional cardiac irregularities that are initiated by reflex stimuli from diseased viscera. It has been shown experimentally that stimulation of the heart nerves will not provoke extrasystoles or auricular fibrillation unless favoring circumstances, such as some toxic injury of the myocardium coëxist.[17] Clinical experience supports this observation, for neurogenic cardiac irregularities are the exception, not the rule, when the cardiac nerves are reflexly stimulated. It is a common observation that in patients who are subject to extrasystoles the ectopic beats may be produced by exercise. They appear most frequently during the subsequent slowing of the heart, but may also arise during the period of acceleration. Smith and Moody[18] described several patients in whom forced breathing caused extrasystoles during the period of maximum vagus effect. In one case this maneuver initiated an attack of auricular fibrillation. Wenckebach[19] observed a patient in whom extrasystoles were regularly produced when he swallowed a dry crust of bread. Another case has been reported in which swallowing initiated paroxysms of tachycardia.[20] Other apparent reflex causes of paroxysmal tachycardia have been mediastinal glands in Hodgkin's disease,[21] and the insufflation of air into the uterus and Fallopian tubes.[22] Extrasystoles,[23] as well as transient auricular fibrillation[24] accompanying gall-bladder disease, appendicitis and duodenal ulcer, and disappearing following operative treatment of the abdominal condition, fall in the same class. In these patients, a toxemia may favor the appearance of these irregularities. The onset of paroxysmal

auricular fibrillation, tachycardia, or flutter during anesthesia, may be explained in the same manner.[25]

Finally, reflex stimulation of the cardiac centers from the brain is a most important cause of neurogenic heart disease. The influence of mental and emotional states on the heart is common knowledge. It is less often realized that psychic stimuli may provoke extrasystoles[26] or even paroxysmal tachycardia.[27] The anxiety neuroses, indeed the varied psychic disturbances that contribute so largely to the development of the picture of neurocirculatory asthenia may be regarded as producing excessive and exaggerated stimuli which reflexly affect the heart through the corticomedullary pathways whose course is still unknown.

Of equal importance are cardiac disorders due to increased irritability of the visceral nervous system. Such a state of so-called "autonomic imbalance," is often hereditary and constitutional. Again, it not infrequently follows severe infectious disease such as pneumonia or influenza; or may accompany disturbances of the internal secretory glands, as in Graves' disease and in the menopause. In all of these conditions, the symptomatology is much the same, except that in the constitutional cases the disorders are usually more severe and persistent. The symptoms are not restricted to the heart, but are often referred to the gastrointestinal tract, the brain, and the vasomotor system as well. Indeed, it is often impossible to determine to what extent the cardiac disorder is due simply to increased irritability of the extrinsic nervous apparatus of the heart, and to what degree it is secondary to neurogenic vasomotor disorders, or to an increase of afferent stimuli from the brain, for as a rule all three factors operate together. For this reason, all three groups must be considered together in a discussion of the symptomatology. They are distinguished from one another in order to emphasize the varying physiologic mechanisms that are at play.

Increased autonomic irritability on the sensory side makes the patient aware of the normal beat of his heart and arteries; it may give rise to palpitation and heart pain. Furthermore, the afferent stimuli that arise from the normal functions of the body and that in health enable the heart to adapt the circulation to the needs of the moment, as well as the excessive afferent stimuli arising from the associated mental and gastrointestinal disturbances, give rise to unregulated motor reactions of the heart. In addition there is the dynamic effect of the accompanying vasomotor disorders, which has not, to my knowledge, received proper emphasis. In these patients the acrocyanosis, which is usually present, is but symptomatic of a general vasomotor incoördination. As a result of the disturbed innervation of the bloodvessels, the capillaries and venules in the splanchnic region and in other areas of the body are dilated and a large amount of blood becomes pooled in them. Consequently, there often is an inadequate amount of blood in the left ventricle

and in the arterial tree. This lack makes itself felt particularly during and after exercise and undoubtedly contributes largely to the rapid pulse, the dyspnea and sense of exhaustion which follow physical exertion. It accounts too for the frequent attacks of vertigo and fainting.

It must be apparent how closely interwoven these several elements are in any particular case—increased afferent stimuli from a disordered psyche, increased irritability of the visceral nervous system and the circulatory disturbance secondary to the accompanying vasomotor disorder. Yet at times, they may be clearly distinguished. The patient who develops all kinds of symptoms referable to his heart, after an unwise physician has told him that he has a heart murmur and must be very careful of himself, is suffering from overactive cardiac reflexes initiated by his worrisome mind. The convalescent from pneumonia, who complains of palpitation, precordial pain, and dyspnea, is suffering from increased irritability of the nervous mechanism of his heart. The asthenic individual with cold hands and feet and a long, narrow thorax is probably suffering primarily from poor blood distribution due to a disturbed vasomotor control. But it will bear repetition, that in most instances all three factors are simultaneously operative.

Conclusion. The diagnosis of neurogenic heart disease must be made primarily by the method of exclusion, by eliminating every possible organic cause for the cardiac symptoms. The positive signs of neurogenic heart disease do not differ from those found in other cardiac disturbances. They consist of the subjective symptoms of dyspnea, precordial pain and palpitation, and the objective signs of tachycardia, instability of heart rate, precordial hyperesthesia and acrocyanosis. In this brief presentation, no attempt has been made to discuss the symptomatology of neurogenic cardiovascular disorders. I have tried rather to point out the mechanisms underlying these disturbances. Successful therapy depends on the study of each individual patient in the light of his disturbed physiologic processes.

Cardiac disorders due to focal lesions involving the heart nerves or nuclei are rare. Neurogenic disorders of the heart arise from increased activity of the reflex arcs as a result of excessive or exaggerated afferent stimuli, of increased irritability of the visceral nervous system of unknown localization, or they may be determined by altered blood distribution caused by neurogenic vasomotor disorders.

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THE TRANSMISSION OF SOUNDS THROUGH THE CHEST.

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This article attempts to answer briefly the question, What are some of the fundamental principles involved in the transmission of sounds from within the respiratory tract to the chest surface? More specifically the problem is, to determine why so much sound is lost in transit through the chest, and why sounds of different frequencies are affected differently. In the investigation, valuable help has been derived from medical and acoustic literature, from the very generous coöperation of physicians, physicists and others, from

clinical and autopsy data, and from animal and other experimentation.

The Nature of Sound. Sound exists physically as a form of vibrational energy present in one or more elastic material media, and, under suitable conditions, for example, of pitch and intensity, is capable of exciting the sensation of hearing, and, less generally, of feeling. Three kinds of sound vibrations will be mentioned: (1) The free vibrations of elastic bodies vibrating at their proper frequencies and manifested as stationary waves, as exemplified in the free vibrations of vocal cords, of violin strings, of air in an organ pipe, and of any sonorous body when struck. (2) Forced vibrations, in which the vibrations of a body respond conformably to and depend upon a periodic force, such as that of recurring sound waves, which force may or may not differ in frequency from that of the free period of the body excited. These vibrations may vary in frequency and be discontinuous. Stationary waves are often present. Examples are found in the forced vibrations of the ear drum, of telephone and phonograph discs, of the diaphragm of the Bowles' stethoscope, of sounding boards, of films of soap suds and soap bubbles, and of the walls of inflated balloons and of air vesicles of the lung. When the actuating force has the same, or nearly the same, frequency as the free period of the responding body, sympathetic vibrations are said to result. (3) Longitudinal or compressional sound waves, manifested in a successive spreading out of alternate condensations and rarefactions of particles or molecules in certain homogeneous media. This is the method by which sounds usually reach the ear.

The Origin of Sounds. Sounds are traceable to the vibrations of sounding or sonorous or vibratile bodies, which vibrate as either forced or free vibrations. Sounding bodies may add to or reënforce the original sounds. The term resonance is often used as synonymous with sympathetic vibration, especially if there is reënforcement, though popularly it is used for any reënforcement due to a periodically acting force. Sounding bodies may be excited to vibration by any of the three kinds of vibrations above mentioned, by movements of air, by percussion, and by other means. Sounding bodies may ordinarily vibrate at many frequencies, as in the case of sounding boards, at a rather limited number, like the lung, or chiefly at one frequency, as with the tuning fork.

The Transmission of Sounds. Sounds may be transmitted through the chest by free vibrations, by forced vibrations, and by ordinary sound waves which occur in homogeneous media under suitable circumstances. When sound is transmitted, the energy of vibrational motion and of elastic compression is exhibited. Friction also is present generating heat, but is not a vibratory sound energy. It represents the reduction of sound energy transmitted.

Simple and Complex Sounds. Simple sounds have a single rate of vibration. Complex sounds are composed of simple sounds of

different frequencies. Most sounds are complex. The individual simple sounds of a complex sound are subject to change independently. Thus the low- and high-pitched sounds of the voice are influenced differently by the tissues of the normal lung.

Sound Intensity. The intensity of a simple sound varies as the product of the squares of its amplitude and frequency. The intensity of a complex sound is equal to the sum of the intensity of its component simple sounds.

Sound Pitch. With simple sounds this depends on the rate of vibration. The pitch of a complex sound is usually the pitch of its fundamental tone, but to determine this is impossible for most people. In medical terminology, one sound is often said to be higher pitched than another when it contains relatively more sound that is high pitched, even though the fundamental is the same, as in the case of the vocal resonance over solid and normal lung.

The Unequal Transmission of Sounds through the Chest. Between the interior of the air passages and the chest surface different frequencies, even with the same initial intensity, are apt to be affected unequally, with the result that some sounds are transmitted better than others. This is the rule normally and is frequently manifested under abnormal conditions. Slight unequal transmission of different frequencies doubtless often escapes detection. To account for the discrepancy occurring normally, it has been suggested that the higher-pitched sounds may be absorbed by resonance within the minute air spaces of the lung, an explanation still lacking confirmation. Animals' lungs outside the body in various stages of inflation do not transmit the low-pitched sounds better than the high pitched ones. The absorption of sound energy by resonance seems more likely to occur in the transmission of sounds through the abdomen, which commonly gives a percussion note of about 300 vibrations per second, and often transmits sounds of 128 vibrations per second more clearly than those of 256 vibrations per second, and much more plainly than those of 512 vibrations per second, the tests being made by applying tuning forks directly to the abdomen, or to some interposed object, while the stethoscope (preferably a Bowles' stethoscope) is placed at some diagonally opposite point of the abdomen. How much the different thoracic structures and contents vibrate as stationary waves in their individual parts, and how much in various combinations of separate parts, in sound transmission, is somewhat conjectural.

Sound Transmission through the Normal Chest. Air-borne sounds of suitable energy and frequency, like the low-pitched simple sounds of the voice, even if relatively feeble, may set into forced vibration, and also, under favorable conditions, into sympathetic vibration, suitable tissues rendered susceptible by proper association with air, such as the normal lung tissues, even while higher-pitched sounds are being totally obstructed by reflection. This tissue response to even

relatively loud sounds of suitable pitch within the air passages, though important in auscultation, is actually so feeble as to be undetected by the unaided ear separated from the chest wall. There is no appreciable reënforcement from the tissue vibrations or other sources, not even of the voice itself, which is contrary to a quite prevalent opinion. Vocal sounds might be reënforced external to the air passages if the chest contained simply air instead of spongy lung. Air-borne sounds are only feebly resonated by solids even when the latter are very sonorous, which is far from being true of the lung and chest wall, as tested by percussion and direct application of vibrating tuning forks. Vocal sounds from the mouth encountering the exterior of the chest excite very weak response. Extensive pulmonary and pleural involvement does not affect the resonance of the voice. The marked normal diminution of all the original sounds in the air passages by reflection as they attempt to pass between the air and the tissues is only slightly counteracted by the limited vibrancy of the tissues in the case of the favored sounds. The normal breath sounds also set the chest wall into vibration.

The fundamental tone of the normal pulmonary percussion note and of the normal vesicular breathing has a frequency of about 108 vibrations a second, corresponding to the frequency of the voice sounds that are transmitted most favorably through the normal chest. The average man's speaking voice—nearly 128 vibrations per second for the fundamental tone—gives a relatively intense vocal fremitus and vocal resonance, while the average woman's speaking voice—nearly 256 vibrations per second or "middle C"—gives a much less intense vocal fremitus and vocal resonance, the latter being also higher pitched in women. At some point above 256, and probably nearer this than 512, vocal sounds cease to be transmitted. (Touch readily detects vibrations over the larynx with a frequency above 512.) This special responsiveness to low-pitched sounds seems to reside in the lung rather than in the chest wall, which normally does not very specially favor the transmission of low-pitched sounds as tested by tuning forks applied to the chest. A wet sponge of suitable character also transmits frequencies of about 128 better than those of 256, as tested by sounds from tuning forks applied directly to the sponge, or through some interposed object. On the other hand, low-pitched sounds are not transmitted much better than high-pitched ones through a dry sponge, or aërated gelatin, or soap suds, or an inflated sheep's lung outside the body. This lung gives a percussion note and artificial breath sounds predominantly higher-pitched than the normal chest sounds, perhaps chiefly due to the relative anemia of the lung, the blood in the normal lung inside the body presumably acting as a weight on the tissues and slowing their vibrations.

Sound transmission through the chest by means of tissues vibrating in unison with sounds from within the air passages is most

effective when both lung and chest wall are readily vibratile and in contact. This may occur normally when the percussion note is loud, as in the thin-chested and in children, and abnormally when a partially collapsed but aërated lung underlies the chest wall. Unfavorable conditions exist when the chest wall is thick, when, theoretically, the lung tissues have lost much of their elasticity, when the lung is solid, and when the pleural cavity contains fluid or air. Normally the degree of vibratility of the chest wall itself may be revealed crudely by the intensity of the percussion note properly elicited, and also by contrasting the different effects of light and firm pressure by the bell of the stethoscope on the intensity of the voice and breath sounds. It is believed, however as already said, that the selective preference for low-pitched sounds is a peculiarity of the normal lung rather than of the overlying chest wall.

Sounds within the Respiratory Tract. Over the larynx are heard normally: (1) Vocal sounds consisting of weak vocal-cord vibrations (or periodic puffs of air from the glottis, according to Willis) both fundamentals and overtones, amplified by chambers chiefly above the trachea, mingled with sounds arising at the lips, teeth, and so forth; (2) whispered sounds, which much resemble the vocal ones except that the vocal cords are partially relaxed instead of being tense; (3) breath sounds. Intralaryngeal simple sounds of proper pitch may be resonated by chambers below the larynx, such as the bronchi or cavities communicating with bronchi. This resonance does not appreciably influence the voice itself, but may be strikingly manifest over the chest in certain pathologic conditions. The normal inspiratory murmur arises in the lungs, perhaps from vibrations of the delicate pulmonary membranes excited by air movements. Normal expiration frequently has a pulmonary origin, but may be supplemented or replaced by laryngeal sounds especially in children. Râles arise in various parts of the respiratory tract and may be resonated within it. They are exposed to the same conditions on transmission as are other sounds.

Sound Reflection. Sounds from within the larynx usually reach the chest surface with but a trifle of their former intensity, both in health and disease, however favorable the conditions for transmission. Most of the loss is effected between media of such different densities as air and tissue or air and fluid, and is due largely to the reflection of sounds. There is no appreciable loss between fluid and tissue. Air, fluid and tissue are each of them elastic media and good sound conductors. Conditions for reflection occur normally between the interior of air passages and their walls, between air in the peripheral alveoli and the overlying chest wall, and, to a less extent, between the chest wall and the air outside it. Reflection is also caused by tense membranes adjoining air like the normally expanded lung tissues. As these relax reflection becomes reduced. Susceptible vibrating tissues reflect low-pitched air-borne sounds

slightly less than high-pitched ones. A thin layer of aërated lung between the chest wall and solid lung or a cavity may reflect all the distinctive, characteristic sounds. Reflection is specially marked in cases of pneumothorax.

Conversely, reflection by the walls of the air passages actually carries considerable sound energy deeply into the lung, at the same time offering a large surface whence sounds can extend peripherally. When an air passage is completely blocked sounds fail to pass beyond the obstruction because of reflection, unless the area affected transmits sounds directly across to the chest surface from the trachea or other air passage proximal to the obstruction, as may occur in cases of pleural fluid or consolidation including massive atelectasis.

Diminished Vibratility of the Tissues. Conditions interfering with the vibratility of the tissues increase the reflection and decrease the transmission of low-pitched simple sounds previously favored. This often occurs with solid lung, being readily and frequently observable in the diminished vocal fremitus of men, and is even more marked over fluid. Simultaneously higher-pitched sounds may come through louder than normal because for them the reflection may be actually reduced below the normal. Sounds of all frequencies are then affected much alike.

Sound Diffusion or Dispersion. Sound energy under favorable conditions varies inversely as the square of the distance from the source. The weakening of sound through its widespread radiation or scattering is familiar to all. It influences physical signs chiefly in some cases of pleural fluid.

Diminution of Normal Breath Sounds. This is not due ordinarily to deficient conduction but to failure of production, as in early stages of inflammation of the lung or pleura, when the vocal resonance may be normal.

Sound Absorption and Disappearance. The transference of sound into other forms of energy in the chest is probably associated largely with reflection.

Increased Sound Transmission. A collapsed but aërated lung reflects sounds less than does a normal one. If it is overlaid by chest wall the latter is usually more vibratile than normal. Solid lung and fluid may yield high-pitched sounds absent in health, owing to their lessened reflection, while lower-pitched sounds may be weaker because the lung and chest wall are less vibratile. Patulous openings in the lung or chest wall greatly reduce reflection.

Application of Principles to Chest Conditions. What has already been said will now be applied to six typical chest conditions.

1. *Normal Lung.* The only sounds from within the larynx to reach most of the chest surface in many normal adults are the lower-pitched simple sounds of the voice. These are able to excite the lung into forced vibration and thereby slightly overcome the reflection which often totally obstructs higher-pitched sounds.

Consequently the vocal resonance lacks the distinctive characteristics of speech, while the laryngeal whisper and breath sounds are often inaudible. The normal breath sounds arise chiefly or wholly in the lungs, perhaps in the vibrations of the delicate pulmonary tissues, and set the chest wall into vibration, though too feebly to be felt.

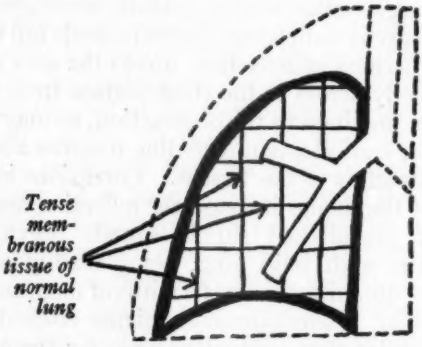

FIG. 1.—Normal lung. Laryngeal sounds are mostly eliminated by reflection except the lower-pitched vocal sounds. These excite the pulmonary membranes to selective vibratory response. The chest wall, if not too thick, is relatively vibratile and conductive to sounds, but less so than if the adjacent lung is collapsed and air-bearing.

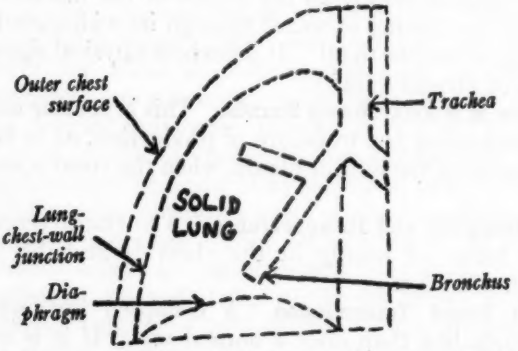

FIG. 2.—Solid lung. All laryngeal sounds are affected much alike, the lower-pitched ones being less favored than normally and the higher-pitched ones more so. There is little or no reflection or special selective responsiveness external to the air passages. The chest wall is less vibratile and conductive than normal. Pulmonary breath sounds are not produced.

2. *Partially Collapsed Lung.* The more or less relaxed and contracted but still aërated lung occurs typically over several interspaces anteriorly above some large fluid collections. Reduced tension of the lung tissues lessens reflection of sounds in general. Increased vibratility of the overlying chest wall, indicated by the increased intensity of the percussion note, favors better sound transmission. The vocal resonance is often louder than normal and

contains more high-pitched sounds. Rather weak whisper and laryngeal breath sounds are common. Breath sounds originate in the lung only if it is expanding.

3. *Solid Lung.* The spoken, whispered and breath sounds from the larynx lose most of their energy in passing from within the air

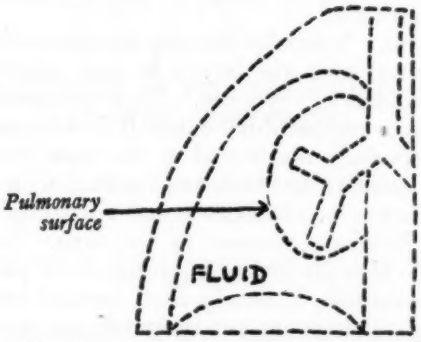

FIG. 3.—Pleural fluid. Lung solid. Lower-pitched laryngeal sounds are diminished because the lung is solid and the media external to it are less vibratile and conductive than normal. Diffusion, when effective, is so chiefly below the lowest part of the lung. Higher-pitched sounds are often audible because there is little reflection either within the lung or at its contact with the fluid.

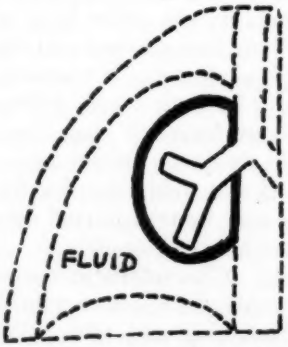

FIG. 4.—Pleural fluid. Lung collapsed but air-bearing. Lower-pitched laryngeal sounds are diminished because the media external to the lung are less vibratile and conductive than the normal chest wall. Reflection within the lung is reduced, so that higher-pitched sounds may sufficiently overcome the reflection at the lung-fluid junction to become audible peripherally.

(Figs. 1, 2, 3 and 4 from 10th Annual Report, Phipps Institute, Philadelphia.)

passages to the completely solidified lung, that is, from air to tissue or its equivalent, but from thence to the chest surface loss is negligible. Sounds of all pitches appear to be affected much alike, and the homogeneous lung responds selectively to special frequencies little if at all. The normal low-pitched sounds are actually reduced, which may diminish the vocal fremitus even when the vocal reson-

ance is increased, because the hand does not recognize the higher-pitched sounds present in the vocal resonance. Comparably over the back of the neck the low-pitched sounds may be less intense and the high-pitched ones more intense than over the normal lung. The high-pitched sounds include the characteristic bronchial sounds audible during speaking, breathing and whispering. Normal breath sounds are not produced.

4. *Pleural Fluid.* Normally the only sounds audible all over the lungs to be derived from the larynx in most adults are the low-pitched simple sounds of the voice. These are greatly diminished or are absent over pleural fluid unless it is adequately localized. The change is specially manifested in the vocal fremitus of men. The paramount cause is the contact of the fluid with the chest wall, which greatly lessens or abolishes tissue vibratility and the associated forced vibrations external to the lung. Sounds may be audible when too high pitched or too feeble to be palpable. Diffusion, when demonstable, is usually most marked below the lowest part of the lung. Pulmonary breath sounds are produced feebly if at all.

Over the fluid itself the vocal resonance, whisper and breath sounds often suggest a pneumonia because of improved conduction of high-pitched sounds, which may be widespread even when the pleural cavity contains over 2 liters of fluid. If the lung back of the fluid is solid, sounds do not suffer from reflection appreciably more than if the solid lung is in contact with the chest wall. If the lung back of the fluid is air-bearing, it transmits sounds better than if normally expanded. In both cases, high-pitched sounds may enter the fluid with more intensity than they normally enter the chest wall. Once in the fluid they are not again exposed to reflection of any importance. If the fluid occupies the upper part of the pleural cavity, sounds may be transmitted directly across from the trachea or perhaps from a large bronchus.

5. *Pulmonary Cavity.* Characteristic cavernous and amphoric sounds may result when cavities resonate suitable simple sounds from the voice, whisper, breathing and râles. Whether these sounds actually reach the chest surface depends on the conditions for transmission. Very little aërated tissue between a cavity and the chest wall is sufficient to block by reflection the distinctive high-pitched sounds and obscure the diagnosis. Relatively good conduction occurs if the cavity is directly in contact with the chest wall, or is separated from it by solid lung.

6. *Pneumothorax.* In this condition, absence or marked loss of transmitted sound occurs however slight the amount of air in the pneumothorax cavity, provided it is spread over a sufficiently extensive area, and if no patulous opening exists anywhere. Marked reflection is produced when sounds within the air passages encounter the lung, though less if the lung is collapsed and air-bearing, and

there is also marked loss as they pass from the lung to the pneumothorax cavity, where sounds of suitable pitch may be resonated. All sounds suffer markedly from reflection on reaching the chest wall. The characteristic quality of the sounds, when present, is due to resonance by the pneumothorax cavity or some part of it, of simple sounds of suitable pitch derived from the voice, whisper, breathing, râles, and, it may be added, from the tapping of coins.

CORONARY OCCLUSION IN BUERGER'S DISEASE (THROMBOANGIITIS OBLITERANS).

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The autopsy material in thromboangiitis obliterans is exceedingly small. I was surprised to find that Buerger[1] in his book reported only 4 autopsies done on the cases under his observation. I have looked through the literature back to 1916 and have found but one reference with autopsy report.[2] The recent report of Allen and Brown[3] from the Mayo Clinic of 200 cases makes no reference to any autopsy findings. Because of this paucity of material, it becomes highly desirable to put on record every bit of information that can be obtained postmortem, even when death has occurred a number of years after the amputation of the affected limb. We do not know that the etiologic factor ceases to operate after the ablation of the painful or gangrenous part. We have no reason for assuming that it does. We may also very well inquire whether the characteristic process is confined to the vessels of the extremities. Buerger says: "Little is known regarding the participation of the arteries other than those of the extremities in the characteristic process. . . . The literature is practically devoid of reliable information on this point." "The fact that in the autopsy material at our disposal the lesions of thromboangiitis obliterans were confined to the vessels of the extremities might lead to much speculation and critical query. It would mean that local predisposing factors must needs be requisite for the special susceptibility of these vascular territories." Again if the characteristic process is confined to the vessels of the extremities, may the underlying causative agent not predispose the vessels of other parts of the body to other forms of disease, namely, chiefly atherosclerosis? As Buerger points out, there is need of great care in interpreting an arterial lesion found at autopsy years after the amputation for during the intervening time intercurrent affections, atherosclerosis and secondary thrombosis could play a rôle in

producing a similar pathologic picture. It is striking, however, that of the only 5 autopsies on patients with Buerger's disease which I have been able to find (4 by Buerger and 1 by Perla,[2]) an affection of the coronary arteries was noted in 3. The case which I am now reporting makes a fourth. A summary of the other 3 cases is as follows:

Case Reports.—1. (Buerger[1]) Thromboangiitis; precocious atherosclerosis; coronary artery disease; sudden exitus. Male, aged twenty-four years (November, 1907), amputation of the left big toe for gangrene November 6, 1907. Amputation at the left knee because of the failure of the wound to heal, May 9, 1908. Amputation of the right leg at the middle third for impending gangrene March 1, 1909. Amputation of the right thigh because of pain and ulceration in the right stump, May 29, 1911. Sudden death afterward. The autopsy showed heart muscle very brown with yellow areas of degeneration throughout it and other areas of more or less circumscribed fibrosis. Such lesions were found only in the wall of the left ventricle and not in that of the right. Left coronary artery was normal for about 1.5 cm. from its origin, then the main branch running down to supply the left ventricle was found to be more or less filled by fibrous yellowish-white substance adherent to the wall and dividing the lumen of the vessel into two very small parts (recanalization?). This fibrous process in the lumen of the vessel could be traced down for about 3 cm. when the vessel was lost. Right coronary arteries and veins showed no such change. Atherosclerotic plaque was found on the right posterior sinus of Valsalva encroaching upon the lumen of the orifice of the right coronary, reducing it to a pin point. Numerous pinhead and slightly larger atherosclerotic patches were scattered profusely beneath the intima of the aorta.

2. (Buerger[1]) Thromboangiitis; extensive atherosclerosis; bland thrombosis in aorta, celiac axis, superior mesenteric arteries; exitus. Male, aged twenty-one years, amputation of left thigh. Usual lesions of thromboangiitis obliterans were found in vessels of extremities, even at the site of ablation in popliteal artery. Death five days later. Autopsy showed extensive thrombosis of femoral artery, external iliac, celiac axis and superior mesenteric arteries with a gangrenous gut. There were mural thrombi in the aorta and numerous infarcts in the spleen, kidneys and heart. *Coronary vessels showed very marked atheroma;* the entire intima presented numerous raised patches. Here and there, however, were small button-like elevations due to nodules in the media of the vessels over which the intima appeared perfectly normal.

3. (Perla[2]) Male, at the age of twenty-eight years amputation of the left foot in 1901 because of pain and gangrene. Pain persisted and gangrene spread. Midtibial amputation in January, 1902. Patient was free from all symptoms in this leg for fifteen years. In 1917, the entire stump began to pain, feel cold and became dark blue. Seven months later—June, 1917—amputation above the knee for gangrene. In the meantime, in 1902, paresthesia, cold sensation, cyanosis and gangrene of the right leg. Amputation through the upper third of the right tibia in January, 1903. Gangrene of the right ring finger in 1914, requiring amputation. In 1917, at the age of forty-four years, he was admitted with pains in both stumps and a gangrenous patch on the right stump. The right hand had a purplish hue and became deeply cyanotic when lowered. When the arm was raised, the entire hand became rapidly pale. The left hand showed the same changes. The patient was orthopneic and cyanotic. In January, 1918, amputation of the left index finger. In March, 1918, amputation of the right leg in the middle of the thigh, healing with difficulty. In January, 1920, amputation of the left hand. In October, 1920, the patient vomited twice, became

cyanotic and died suddenly within a few minutes. Autopsy showed a thromboangiitis obliterans (organized canalized thrombi) involving the arteries of all extremities, including external iliac arteries and *left coronary artery*. "Beginning 1½ cm. from its orifice in the aorta the main left coronary artery showed an organized canalized thrombus almost completely occluding the lumen for a distance of 1½ cm. The process here resembled that in the vessels of the extremities. The right coronary artery showed no abnormalities. On section the left myocardium and the muscle in general showed no appreciable abnormalities."

My own case is as follows: H. S., male, aged fifty-five years, Jew, born in Hungary, in America thirty-three years, salesman, was admitted to Touro Infirmary March 2, 1921. Four years previously when he was fifty-one years of age, he had had gangrene of the right foot necessitating amputation at the ankle and two weeks later at the junction of the upper and middle third of the thigh. Other than malaria fever twenty years previously, he had had no serious illness. He denied all venereal disease. In December, 1920, he began having pains in the big toe of the remaining foot. The sensation was like pins being stuck in the toe. About one week before his admission he noticed a "sore" on the medial aspect of the base of this toe. On his admission he had pains also in the little toe though less marked than in the big toe. He also had a "sore" under the little toe.

After several weeks, during which Ringer's solution was given repeatedly by hypodermoclysis, Professor Matas determined to attempt to give him some relief by doing a periarterial sympathectomy according to the plan of Leriche. Dr. Matas' notes at the time of the operation, April 15, 1921, were as follows:

"Case of presenile gangrene, right foot, causing progressive ischemia of the foot and especially the toes, menacing an approaching gangrene. The patient suffers constantly and intensely with causalgia, a burning pain in the toes and foot. He has lost the opposite leg by amputation. The object of the operation today was three-fold: (1) To determine the limit of the ischemia in the leg and foot by the Moskowicz test; (2) to do a periarterial sympathectomy of Leriche, and (3) to obliterate the accompanying veins in order to obtain hemostasis of the peripheral parts on the von Oppel plan. The Moskowicz test plainly showed that the vascular supply of the limb was very scant and the circulation extremely feeble from the middle of the leg to the toes. Nearly two minutes elapsed before the tip of the toes and the dorsum of the foot assumed a living color. The hyperemia blush never did go below the knee, and large, cadaverically pale areas persisted for a long time in the lower leg and dorsum of the foot. The posterior tibial artery and satellite vein were first exposed behind the internal malleolus and the artery was found completely obliterated for a very considerable length of its course. The two satellite veins, however, were pervious. It was then decided that in view of the obliteration of the artery, the simplest way of performing a periarterial sympathectomy was to excise a segment of the artery including its sheath. Following this idea, 1½ cm. of the obliterated artery was excised together with the corresponding length of the accompanying vein.

"The dorsalis pedis was found obliterated precisely in the same way, appearing as a hard, chalky cord. This also was excised with the venæ comites, the same length, about 1½ cm. The wounds were closed with a few interrupted catgut sutures. The toes and anterior part of the foot seemed to be quite pink and almost hyperemic up to the time when the foot was wrapped up in cotton wadding."

On May 6, 1921, Dr. Lucian Landry did an amputation at the junction of the middle and lower left third of the left leg. Anterior and posterior tibial arteries were found to be very much reduced in caliber. On June 9, 1921, Dr. Landry did a circular amputation at the junction of the middle and lower third of the thigh. The main vessel was found to be very much

thickened and a small amount of laminated clot was removed from within the vessel.

On July 28, 1921, Dr. Urban Maes found it necessary to incise and drain an abscess in the amputation stump. Following this the patient seems to have progressed without further trouble. For the next four years the patient remained as an inmate of Touro Infirmary to which there is attached a "true" infirmary for infirm Jews. He was also comfortable and cheerful. He refused to wear the artificial limbs provided for him and spent his time in a special rolling chair.

During the night of November 23, 1927, he was startled by finding another patient bending over him. This latter was a doctor who had suddenly become disoriented and was trying to make a physical examination of our patient. Shortly after this H. S. complained of a burning sensation and pain in the heart. He had a very uncomfortable night and could not sleep until he was transferred to another ward. The next morning he arose as usual—took breakfast and dinner and was out of the ward. At 5.30 P.M., however, he again complained of pain in the region of the heart and refused his supper. At 7.30 P.M. he was given codein ½ gr. and was quiet after this but did not sleep. At 1 A.M. he vomited, was cold and clammy and his respiration was difficult. Respiration was 32 but his pulse was only 80. Half an hour later he vomited again and a little later the nurse recorded his pulse as being a trifle irregular and rather weak. At 3 A.M. he received a hypodermic of morphin, soon after which he vomited again. At 3.30 A. M. he started to vomit and cough and in doing so lost his balance and fell out of bed. At 5.30 A.M. he complained of pain in the abdomen and that his bowels would not act. The abdomen was distended. The pulse was 80, very weak but quite regular, respiration 32. At 7.30 A.M. his temperature was 97°, pulse 100, respiration 20 and his limbs were cold. At 9 A.M. the pulse was very weak—could be felt only at times. At 9.35 the bowels moved. At 10.30 he had another large bowel movement. I saw him for the first time immediately after this. He had just removed himself from the bedpan by raising himself on his hands. I comment upon this to indicate his great strength. It is to be remembered that he had no legs. He was sitting erect. My first impression was that he was not very ill. I was shocked, however, to discover that I could not feel his pulse nor hear his heart. It was impossible to ascertain his blood pressure by the auscultatory method at the elbow. The chest was moderately hyperresonant—the breathing slightly asthmatic. The patient did not cough nor complain of dyspnea. His only complaint was of pain in the abdomen. The abdomen was rounded and somewhat protuberant, slightly more tender and resistant on the right than on the left side. No masses nor organs could be made out. Intracardiac injection of 1 cc. of 1 to 1000 epinephrin had the effect within three minutes of producing a feeble, weak pulse at the radial, rate 56. This varied between 44 and 60 for twenty-five minutes. The injection was then repeated and the pulse rate immediately rose to 120 but within a minute fell to 96. In spite of morphin the facial expression indicated great agony. The patient continued practically pulseless until his death at 1.45 P.M. He was very restless and kept trying to sit up. Finally, he sat up suddenly, vomited a large quantity of brownish fluid and was dead.

Autopsy by Dr. J. A. Lanford. The body is that of an exceedingly well-developed and powerful white male about sixty-two years of age. Both lower limbs have been amputated at the junction of the upper and middle thirds of the thigh and old well-healed stumps remain. The skin is elastic and unjaundiced. There are embalming wounds in the axilla and in the abdomen. No superficial adenopathy evident.

Thorax. The pleural sacs are free of fluid. There are a few adhesions posteriorly at the apices of both lungs. The lungs themselves are mottled

gray with considerable anthracosis evident. They are quite crepitant and voluminous to the touch.

Pericardial Cavity. The normal amount of clear straw-colored fluid is present. The heart is fixed by preservatives, which have also probably browned the musculature to some extent. The organ contains about the normal amount of pericardial fat. The coronaries are much sclerosed. On opening the heart the valves are in rather good condition though there is a calcareous patch on one of the cusps of the aortic valve. The opening of the left coronary is practically occluded by calcareous deposits. Dissection of the right coronary reveals complete occlusion of its branches by a similar process of calcification. The cut surface of the heart wall shows an enormous preponderance of fibrous tissue, in some areas forming distinct grayish patches.

When the aorta is opened, its wall is found very much thickened with numerous large calcareous plaques elevated above the intima. A slight dilatation of the aorta in the region just below its passage into the diaphragm is noted.

The peritoneal cavity is found filled with the embalming fluid. The intestines are collapsed. They appear in their normal relation, show some discoloration but no other evidence of pathology. The appendix is normal and directed down. The spleen shows some old adhesions. Otherwise the peritoneal cavity is negative.

The liver is about normal in size and with the exception of some greenish discoloration in the region of the gall bladder is negative. There is a movable stone in the cystic duct measuring about 1 cm. in diameter.

The spleen on section shows some fibrosis but is otherwise negative.

The kidneys present a similar picture of fibrosis with several cysts on the surface filled with clear straw-colored fluid.

Anatomical Diagnosis. Coronary occlusion; chronic fibrosis and calcification; chronic myocarditis; chronic nephritis; bronchiectasis; atheromatous degeneration of vessels.

Microscopic Diagnosis. Heart: Fragmentation; cloudy swelling; increase in connective tissue; round-cell infiltration—perivascular; coronary artery occluded by thickening of intimal coat which shows hyalinization and fatty changes and some lime salts deposits.

Aorta: Marked arteriosclerosis; fatty degeneration, particularly in media, also some lime salts deposits; chronic periarteritis; the intima and part of the medial coats show marked degenerative changes associated with necrotic areas in which fatty acids are present and in some instances lime salts deposits; the surface shows fibrin; the outer portion of the medial coats shows round-cell infiltration, which is also present in the adventitia.

Lungs: Emphysema; pigmentation.

Liver: Chronic cholangitis; perilobular cirrhosis; excessive fatty degeneration; cloudy swelling; pycnotic changes in many nuclei.

Spleen: Acute splenitis; areas of degeneration; chronic splenitis; amyloid changes; passive congestion; hemorrhagic infarcts; slight fibrosis.

Discussion. The coronary artery in this case did not show the lesion of thromboangiitis obliterans, as did Buerger's first case and Perla's case, but merely extreme atherosclerosis as in Buerger's second case. It is, of course, quite possible, therefore, that the arteriosclerosis in a man, aged fifty-nine years (at the time of his death), stood in no relation at all to the thromboangiitis obliterans which had caused the successive amputations. Attention, however, may be directed to the fact that two of Buerger's autopsies—one in a man aged twenty-one, the other in a man aged thirty-five years—showed precocious arteriosclerosis. The relation of thrombo-

angiitis obliterans to arteriosclerosis both peripheral and central is of great interest and importance. Buerger has found the two kinds of lesions side by side, that of the arteriosclerosis with its degenerative sequelæ, and that of thromboangiitis obliterans. "Occasionally we encounter the precocious development of arteriosclerotic patches in arteries that are the seat of thromboangiitis. We need not wonder at this circumstance, since it is not uncommon to find marked atherosclerosis in relatively young individuals in whom thromboangiitis is never a complication." "Nevertheless it must be admitted that a predisposition to vascular disease (vascular mediocrity or inferiority) as it manifests itself in certain cases, seems to express itself both in a susceptibility to thrombotic lesions as well as to degenerative ones. Certain it is that the autopsy findings in cases of thromboangitis show that the more centrally situated arteries do develop a tendency to atherosclerotic lesions even though the arteries of the extremities show but little sclerosis." It is because of this possible relation of thromboangiitis obliterans to arteriosclerosis and the predisposition of victims of Buerger's disease to involvement of centrally located vessels to lesions of the one type or the other that further studies of these centrally located arteries becomes of the first importance. We are still very far from understanding the etiology of thromboangiitis obliterans. Buerger believes that the disease is of specific toxic origin. Rabinowitz produced vascular lesions in rabbits by injections of organisms obtained from the blood in cases of thromboangiitis obliterans. Others have cultured resected veins in an acute phlebitis with negative results. Excessive tobacco smoking, changed viscosity of the blood, high-salt diet, fly bites, shortened coagulation of the blood have all been blamed. The wide range of these suggestions gives an adequate idea of the absolute lack of knowledge on the subject. The fact that important internal vessels are frequently involved may give a new direction as well as a fresh impetus to investigation of the disease. Is it a coincidence that coronary occlusion should have been found in 4 out of 5 autopsies on victims of thromboangiitis obliterans? Have other clinicians observed in their patients with this disease deaths suggestive of coronary occlusion?

Summary. In thromboangiitis obliterans the pathologic process is probably not limited to the vessels of the extremities. Affection of coronary vessels has been reported by others. Such a case is reported here both because of the paucity of autopsy material in the literature concerning this disease and because of the great importance of bearing in mind the possibility of heart muscle disease in its victims.

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NEUROGENIC MUCOUS COLITIS.

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The clinical condition commonly known as mucous colitis derives its name from one outstanding symptom, the discharge of mucus from the colon. Possibly because of the "neurotic stigma" with which it is often associated, study of the condition has not achieved the place in gastroenterology which its prevalence would seem to justify. Judging from the diversion of opinion among the older prolific writers on mucous colitis and the paucity of reference to it on the part of modern students, one cannot escape the conclusion that it is little understood. The former were about equally divided in their opinions concerning its etiology between inflammation of the colon and an underlying neurosis. Most authors concede the existence of two conditions, constipation and a nervous factor. The uncertainty of the exact mechanism of its etiology, the absence of any pathognomonic signs and consequently frequent failure in its recognition, the lack of success from therapy, and its frequency, lead us to undertake this study.

Fifty cases have been subjected to analysis. The criteria which we required for a diagnosis was a history of the passage of a characteristic type of mucus from the bowel, a distinctive sigmoidoscopic picture, the absence of sufficient inflammation of the colon reasonably to account for the mucus and the association of certain concomitant phenomena which will be discussed.

Routine sigmoidoscopy on all chronic bowel cases has gradually caused us to assign to mucous colitis what we feel may be a pathognomonic picture. In this condition the mucous membrane of the rectum and sigmoid is clear, being free from any exudate or sign of inflammation. It possesses a glistening, glairy, or shining lustrous appearance which usually involves all of the rectum and visible sigmoid. This was extreme in 38 cases. Most cases were examined frequently. In four of them the characteristic appearance was not invariably present. The degree of glariness varied from time to time in some cases while in others it remained unchanged. Eight of the remaining 12 cases had a distinct suggestion of glistening, but it was either not evenly distributed or its intensity was masked by a concomitant catarrhal proctosigmoiditis. In the remaining cases the membrane possessed no suggestion of luster, but clear, non-

inflammatory mucus was observed in the bowel or secured from the excreta. Possibly the shining appearance of the mucosa may not always extend down into the lower sigmoid. But it seems more likely that the overproduction of mucus is not constant but rather occurs intermittently. In most cases there is no change in the color of the mucous membrane. Hyperemia was noted in 9 cases and pallor in 5 cases. The membranes in 2 cases were recorded as hyperemic on one occasion and pale on another.

Mucus. Mucus can best be obtained for examination through the sigmoidoscope. It varies greatly in consistency and color. It may be the color of egg albumen, milky-white or grayish-white. The consistency varies from that of a rather thin fluid to coagulated membrane-like masses. Several types of mucus may be seen in the same bowel. Mucus is often spread over the mucosa in a skein. We have never seen this clear, noninflammatory mucus firmly attached to the mucous membrane. In most cases a cotton applicator will remove the skeins of mucus without causing bleeding or injuring the mucosa.

The microscopic examination of the mucus removed through the sigmoidoscope or obtained from the feces is of much significance. With a little experience one can differentiate the mucus seen in catarrhal affections of the colon from the type associated with neurogenic mucous colitis. In the latter, the mucus is free from evidence of inflammation. Fibrin and pus cells are absent and bacteria are few in number. There are peculiar hyaline-like structures resembling degenerated phagocytic or endothelial cells containing in their protoplasm small amorphous granules which cannot be identified. Hurst,[1] in considering membranous colitis found the membrane to be free from fibrin and consisting of many degenerated cells and debris derived from the epithelial lining of the bowel, occasional red blood cells, isolated nuclei and many bacteria. The absence of signs of inflammation in the ordinary glairy mucus suggests the possibility of a coëxisting inflammatory factor in the membranous cases of the type described by Hurst. Intestinal sand first mentioned by Dieulefoy[2] and confirmed by others in association with mucomembranous colitis was not found in our cases; however, no special search for sand was made. In 10 cases there was a concomitant catarrhal proctitis or proctosigmoiditis of the variety seen in association with proctostasis. In many of these there was, in addition to the clean mucus described above, yellow or brown mucus which was adherent to the rectal mucosa, the removal of which resulted in bleeding in some cases.

Histology and Symptomatology. Thirty-two cases were females and 18 males, a higher incidence of the latter than is usually reported. The age varied from fourteen to fifty-three years, with an average of thirty-six years. The condition is apparently rare in childhood and in old age. Twelve patients (24 per cent) had been operated

upon, 8 apparently unnecessarily for they obtained no relief after operation. Of the latter, 4 had appendectomies for so-called chronic appendicitis, 1 a cholecystectomy, 1 an appendectomy and right oöphorectomy and the remaining 2 had an appendectomy and some operation on the right pelvic adnexa. A feature of our cases was the absence of organic gastrointestinal disease. There was a concomitant duodenal ulcer in 2 cases and 1 case of cholelithiasis. Only 6 per cent of cases had definite organic disease. We could not confirm the association of an arthritic diathesis claimed by de Langenhangen.[3] A previous diagnosis of arthritis, made in one instance, could not be confirmed. We question a greater incidence of mucous colitis in arthritic patients.

The symptoms have been classified for purposes of discussion into pain, disturbances of bowel function, the passage of mucus, dyspepsia, nervous manifestations and constitutional symptoms.

Pain. Nineteen cases (38 per cent) had attacks which might be called mucous colic, that is, abdominal pain usually of a colicy nature followed by a tendency toward diarrhea with the passage of mucus which in most instances was followed by relief from pain. In about one-half of these cases the attack was accompanied by nausea and vomiting. Three patients vomited large quantities of mucus during the attack. Abdominal pain was present in 16 cases (32 per cent) without a definite sequence characteristic of mucous crises. In many of these cases, the pain was relieved or modified by a bowel movement or enema, but this relationship was not constant. The most common situation of the pain was in the lower abdomen on the left side. In 11 cases, for the most part in the colic group, the pain was either generalized or variable in situation. It was most often of a crampy nature in this group. The situation was lower left quadrant, 8 cases; lower abdomen, 6 cases; upper left quadrant, 2 cases; left side, 1 case; umbilical, 2 cases; upper abdomen, 3 cases. The pain was intermittent except in 4 cases, in 3 of which a constant dull pain was present in the left lower quadrant and a fourth in the left upper quadrant. There was tremendous variation in the severity of the pain. In 3 cases with paroxysmal attacks of colic, the pain was extremely severe. Opiates had been used. In 10 cases the pain was severe and in the remainder it varied from mild to moderate. The pain in a few cases was accentuated by eating. Fifteen cases did not complain of pain. This fact cannot be overemphasized as the pain-free cases are often undiagnosed and termed neurotics. Vague abdominal discomfort and dyspepsia was prevalent in the pain-free group.

Bowel Function. Twenty-six cases were obstinately and continuously constipated, 14 cases had alternating constipation and diarrhea. Eight patients had a tendency toward habitual diarrhea and in 4 the bowel function was normal insofar as we could determine. Although we are in accord with the emphasis placed upon

constipation in mucous colitis, we cannot subscribe to the view of de Langenhangen, Hale White[4] and many others that it is almost invariably present. It would appear to be a result rather than a cause of the mucous colitis syndrome. Hurst attributes the spurious diarrhea which may occur to excessive irritation due to constipation. That so-called diarrhea of this type may result from constipation with or without mucous colitis, there can be little doubt. But that diarrhea can be used as an argument in favor of the inflammatory nature of mucous colitis we seriously question. Twenty-four per cent of our cases were not constipated, yet fulfilled all the criteria for a diagnosis of mucous colitis.

Mucus Discharge from the Bowel. The discharge of so-called noninflammatory mucus from the bowel is considered a requisite for the diagnosis. Even this criterion will at times be absent because it has occurred unnoticed by the patient. We would include the discharge of mucus or its recognition in the lower bowel by sigmoidoscopic examination. It is usually of the glairy variety. Pseudomembranous mucus was present in but 9 cases (18 per cent). Two patients who had been passing glairy mucus from the bowel for a considerable period without any history of pain developed painful crises while under observation. The name mucomembranous colitis would seem ill-chosen as the presence or absence of a membrane does not change the underlying condition. The name does not include the majority of cases, in which membranes are not passed, but which are identical with the membranous cases in all other respects.

Dyspepsia. Dyspeptic symptoms were encountered in 29 cases (58 per cent). They constitute a more important part of the picture in the noncolic group although many of the cases with colic were dyspeptic. The most common complaint was gaseous dyspepsia or discomfort attributed to gas, as belching, flatus, fullness and pressure sensations. Nausea, vomiting, pyrosis, anorexia, regurgitation and so-called biliousness were quite frequent. A number of other symptoms probably best described as reflex were not uncommon. Eight patients complained of back pain, 4 of pain in one or both shoulders and a few of neuralgic pains in various situations. Headache and vertigo were very frequent. Palpitation, tachycardia and bearing down sensations were occasionally encountered.

Nervous State. If there is any one phase of mucous colitis about which all writers on the subject are agreed, it is the coëxistence in every case of nervous manifestations. Siredey[5] (1869) and DaCosta[6] (1871) ascribed the condition to neurasthenia. Osler[7] described it as a secretory neurosis. De Langenhangen, White, Cohnheim,[8] Hurst and many others admit a concomitant neurasthenia associated with a catarrh of the bowel. Patients have been variously classified as neuropaths, neurasthenics, psychasthenics, psychoneurotics or neurotics. Many writers have used the terms interchangeably

indicating an absence of any serious effort to classify their nervous status. We are in accord with the view that nervousness of some type is present in practically every case. De Langenhangen mentioned the prevalence of mucous colitis among city dwellers. White found it more common in private practice, that is, in brain workers of the upper and middle classes. In spite of an incidence of 25 per cent of colored patients in our clinic, we have not seen mucous colitis in the colored. Woodward[9] speaks of its increasing incidence after the period of strain of the Civil War and the condition has received a new impetus since the World War.

An effort was made to record the incidence of certain nervous phenomena which seemed more prevalent. Marked emotional instability was present in 23 cases. These patients seemed to be hypersensitive in their contact with others during the ordinary pursuits of life. De Langenhangen uses the expression "excessive nervous impressionability" which seems an admirable one to describe many patients. Our patients were for the most part not neurotic. In fact, many of them were adverse to being called nervous and actually minimized what in some instances seemed to be considerable suffering to avoid the stigma "neurotic." The emotional state approached hysteria in a single case. The emotions seemed to be "nearer the surface" during an exacerbation. The statement, "the amount of mucus in my bowel is a barometer of my nervous state" was made by one patient and the same relationship noted by many. Many authors have stated that sufferers from mucous colitis are always depressed or hypochondriacal. Forty-six per cent of our cases were considered to be depressed. In several patients, cycles of depression occurred simultaneously with attacks of mucus discharge or diarrhea or mucus colic. In 22 patients, a tendency which varied from harmless introspection to grave hypochondriasis was present. Sixteen patients complained of exhaustion or extreme weakness. This symptom was also one which seems to bear more than a usual relationship to local bowel symptoms. Phobias of one type or another, usually visceral, were recorded in 12 cases. Cancer and luetic phobia was most prevalent.

To classify the type of nervous abnormality is not easy. Only 4 patients could be considered to be psychoneurotic and one was a constitutional neuropath. We feel that the local bowel disorder in these 5 cases was entirely independent of their mental state and was dependent upon a vegetative nervous system imbalance which was present in all of them. Janet[10] considers gastrointestinal manifestations like mucous colitis rare in severe forms of psychosis. If such manifestations are present in an individual who afterward develops a psychosis, they will quickly disappear. This author points out that the confirmed neuropath is always better nervously when undergoing strain, exertion, pregnancy, operation or acute illness. The opposite is true of the patient with mucous colitis.

They are made worse by almost any stress or strain, nervous or constitutional. Symptoms were induced or made worse by abdominal operation (5 cases), grief (2), pregnancy (2), excesses in alcohol or tobacco (1), physical exertion (3), menopause (2), menstruation (6), painful abdominal lesion (2), and hives (1). We classified 19 patients as neurasthenic. This does, to be sure, represent a fairly high proportion but by no means is it universally found as many authors claim. Nine patients in the neurasthenic group gave a history of nervous breakdown, most of them having two or more attacks. The remaining 26 patients (52 per cent) we were unable to classify as neurotic, psychoneurotic or neurasthenic, except that their emotional instability might be considered an evidence of a psychoneurotic tendency.

Constitutional Symptoms. Thirty-two patients were of normal weight, 5 were obese and 13 moderately or markedly undernourished. A moderate secondary anemia was found in 7 cases. The average number of erythrocytes for all cases was 4,540,000 per c.mm. and average hemoglobin 85 per cent. A slight elevation of temperature was present in 3 cases during an attack of mucous colic. Mucous colitis may occasionally resemble tuberculous enteritis clinically. It was only after an extensive period of observation that we were able to exclude tuberculosis of the bowel in 2 cases. They were asthenic females, markedly undernourished with signs of healed tuberculosis of the lung, complaining of diarrhea and colicky pain in the abdomen.

Physical Examination. Many authors have stressed the greater incidence of mucous colitis in people of asthenic build. In this series 28 were asthenic (56 per cent), 18 sthenic and 4 hypersthenic (8 per cent). Glenard[11] advanced the theory that mucous colitis was due primarily to splanchnoptosia. Thirty cases were so classified (60 per cent). Splanchnoptosia was absent in too many cases, however, to be considered a primary etiologic factor.

A careful notation was made of the incidence of hypersensitiveness of the abdominal parietes of the type recently emphasized by Carnett.[12] His method was used in the examination for parietal tenderness. Fourteen cases were found to have hypersensitiveness of the abdominal wall. Time does not permit of a discussion of this interesting question, upon which we hope to write later. Colon tenderness was present in 29 of 44 patients. It was most frequently confined to the distal colon (12 cases). The right colon was tender in 9 cases and both the right and left colon in 8 cases.

Stool Analysis. Aside from the presence of mucus, the stool revealed nothing noteworthy. The reaction was acid in 39 per cent, alkaline in 45 per cent and neutral in the remainder. The average color of the stools was lighter than normal. De Langenhangen attributed this tendency to chologenic dysfunction of the liver. There is no evidence to support this view from a study of our cases.

Gram stains of a fecal smear were examined. The flora did not differ from that of a like number of chronic gastrointestinal patients. A search was made for calcium crystals in the stool and urine. This was suggested by the repeatedly mentioned association between vagotonic preponderance and calcium deficiency. Calcium oxalate crystals were found in the urine in 3 cases and in the stool in 1 case.

Studies Bearing upon the Possible Relationship of Mucous Colitis to Imbalance of the Vegetative Nervous System. Since the classical monograph of Eppinger and Hess[13] this relationship has been gaining some recognition. These authors, Pottenger,[14] Aaron,[15] Cawadias[16] and others consider mucous colitis an exhibition of predominance of parasympathetic activity. We know of no analytical study of mucous colitis from this standpoint.

Past Medical History. An inquiry was directed toward a history of the more common lesions which are often associated with, or supposedly due to, autonomic imbalance. A history of urticaria was obtained from 13 patients, an incidence of 26 per cent. Angioneurotic edema occurred twice. There were 2 cases of hay fever. One patient gave a history of asthma. Five patients were subject to periodic attacks of migraine. There seemed to be an increased resistance against acute infectious diseases (for example, typhoid, pneumonia, influenza, and so forth), judging from the past medical history.

Collateral Symptoms. A group of symptoms suggesting vasomotor instability which were frequently encountered were chilly sensations, local or general sensations or warmth or coldness, cold hands and feet, sweating (either localized or general), tremors, itching, local blotches on the skin, palpitation, throbbing and heart consciousness. One or more of these symptoms were present in an overwhelming majority of cases.

Special Physical Findings. The dark complexion was more common, 90 per cent having either brown or black hair. The hair was oily in 47 per cent and dry in 34 per cent of cases. It was of coarse texture in 54 per cent. Observations on the size of the pupils in 31 cases follows: Myosis, 9 cases; mydriasis, 11 cases; normal or variable, 11 cases. A marked oiliness of the skin was noted 14 times and excessive dryness in 3 patients. Nine patients had acne. Two patients had urticaria when examined. The pharyngeal reflex was tested in 31 cases. It was absent in 9, decreased in 4, normal in 10 and increased in 8 cases. Of 28 cases, 54 per cent were considered to have hypersalivation, 14 per cent complained of dry mouth and the remainder were normal. Thyroid enlargement was present in 3 instances, but a true thyroid syndrome was not encountered.

Blood Vascular Signs. Bradycardia was present in only 10 per cent of cases. Blood-pressure readings were recorded in 44 patients. There were 13 cases (30 per cent) showing hypotension, 48 per cent

had normal pressure, and hypertension (moderate for the most part) occurred 10 times (22 per cent). Pallor, flushing, cyanosis, blotchy erythemas, profuse perspiration, slight tremors were very frequently noted during the physical examination. The average leukocyte count in 43 cases was 6600 per c.mm., a slight tendency toward leukopenia. The same may be said of lymphocytosis. We found an average lymphocyte count of 37 per cent in 39 cases. Although some older writers claim an eosinophilic diathesis in so-called vagotonia, such a tendency was absent in this series.

Function of the Stomach. Since certain authors consider the vegetative nervous mechanism an important factor in disturbances of the secretory and motor function of the stomach, 45 cases were subjected to fractional gastric analysis. Hyperchlorhydria was present in 14 cases, normal acidity in 18 cases, hypochlorhydria in 11 cases and achlorhydria in 2 cases. There were no instances of true achylia. The motility of the stomach by this test was considered normal in 27 cases, and delayed in 14 cases. Four patients had hypermotility. Roentgen ray data was available on stomach emptying in 16 cases. It was normal in 12 cases, rapid in 1 case and delayed in 3 cases.

Gastrointestinal Sphincters. Roentgenologic study revealed evidence of cardiospasm in 2 cases and of pylorospasm in 10 cases. In 40 cases in which a record of digital examination of the rectum was made, a spastic anal sphincter was present 14 times (35 per cent). The anal sphincteric tone was considered normal in 20 cases (50 per cent). Six patients had a marked atony of the anal sphincter. There was a slightly increased tendency toward sphincteric spasm judging from observations made upon the cardia, pylorus and anal sphincters.

Roentgenologic Study of the Colon. The colon was studied by barium enema in 38 cases. Marked elongation of the pelvic colon was reported in 17 cases. The right colon was unduly dilated in 16 cases, but dilatation of the left colon was present in but 2 cases. Ptosis of the colon was evident in 47 per cent of cases (18 cases). Evidence of undue spasm was noted 16 times (43 per cent). The distal colon was the usual seat of spasm (11 cases). It is doubtful if this incidence of spasm is any greater than in any similar number of patients with constipation or diarrhea. Little attention has been paid to the Roentgen findings in mucous colitis. Baetjer[17] reported a "spotted or shreddy appearance due to retention of bismuth on the mucous coated surface after emptying the bowel" in several cases. Schwartz[18] made mention of a flecked or marbled appearance due to bismuth-holding clumps of mucus. Crane[19] described a so-called string sign which he considers almost pathognomonic of mucous colitis. Case[20] states that it is possible to get this string appearance in the absence of mucus a short time after evacuation of a barium-filled colon. He mentions the possibility of the same

appearance in catarrhal or ulcerative colitis. In the total number of 38 cases examined by barium enema, including those who also had a mouth meal, a tendency toward string formation was seen in 6 cases but a definite string sign was present in only 1 case. It is unfair for us to express an opinion concerning the frequency of this sign since only 20 cases were observed on the morning of the second day following a barium meal as recommended by Crane. The spotted, shredded appearance was seen in 2 cases. Any Roentgen ray sign dependent upon the presence of mucus in the colon cannot be considered of paramount diagnostic importance in either a positive or negative way. The same appearance may be simulated by mucus due to other conditions. Furthermore, there must be periods in the course of mucous colitis when there is insufficient mucus in the bowel to produce the sign described.

Special Tests for Vegetative Nerve Imbalance. A series of tests were selected which we thought might elucidate the relationship between vegetative imbalance and mucous colitis. Having knowledge of the variations in response to pilocarpin and atropin in autonomic disturbances, they were not used. Two or more tests were carried out on a series of 34 cases (Table I).

Dermographism. This condition has frequently been reported in states of vegetative excitability, often being considered an indication of parasympathetic preponderance. A test was made for its presence in 27 cases. Eighty per cent of patients had definite dermographism. (See Table I.)

Widal Hemoclastic Crisis. In this test, which was advanced as a measure of the proteopexic function of the liver, a positive response consists of a leukopenia and fall in pulse rate and systolic blood pressure, following the ingestion of a glass of milk. There has been no general acceptance of this phenomenon as a test for liver dysfunction. Glaser[21] feels that a positive reaction occurs in vagotonics in the absence of liver dysfunction. He was able to obtain a positive test after rendering certain patients vagotonic with pilocarpin. We recorded the number of leukocytes before, and every twenty minutes for two hours after the ingestion of a glass of milk in 31 cases. Changes in the pulse and blood pressure were too insignificant to record. The reactions were graded. (Table I.) A negative response was present in 7 cases. A digestive leukopenia occurred in 77 per cent of cases (24 cases). Galup[22] found the same proportion of positive responses in a series of asthmatics.

Goetsch[23] Test. Originally advanced as a test for hyperthyroidism, this procedure depends upon a reaction following the injection of adrenalin. Peabody,[24] Lueders[25] and many others have shown that a positive reaction cannot be considered as having any specific significance in the diagnosis of hyperthyroidism. Intravenous injection of adrenalin is supposed to produce an effect on the body identical with central stimulation of the sympathetic nervous system.

TABLE I.—RESULTS OF A SERIES OF TESTS OF THE VEGETATIVE SYSTEM.

Name.	Widal hemoclastic crisis.	Maximum changes produced by Goetsch test.						Loewi adrenalin test.	Basal metabolic rate.	Glucose tolerance.				Pulse rate.	Blood pressure.	Dermographism.	History of urticaria.	Myosis.	Mydriasis.	Pharynx reflex.	Salivation.	Gastric acidity.	Gastric motility.
		Pulse rate.	Systolic blood pressure.	Pulse pressure.	Sugar urine after three hours.	Constitutional reaction.	Reaction.			F.	½ hour.	1½ hours.	2½ hours.										
1	+3	+35	+22	+17	0	+1	+1	√	√	...	...	...	...	61	108/65	+2	0	..	+	Norm.	Hyper.	Norm.	Delay.
2	+3	+16	+25	+22	0	1	Norm.	Neg.	√	...	...	...	...	84	97/57	+3	+	..	+	...	Hyper.		
3	+1	+11	−2	−4	0	0	Absent	Neg.	7	...	...	...	...	65	118/68	+4	+	..	+	Dimin.	...	Hyper.	
4	+3	+ 4	+44	+30	0	+1	+1	Neg.	5	...	...	...	...	84	100/70	+3	0	+	..	Dimin.	Varies	Hyper.	Hyper.
5	+4	+12	+78	+60	0	+1	+2	+1	√	...	...	...	...	84	112/80	√	√	..	+	...	...	Hyper.	
6	+3	+ 8	+30	+18	0	+2	+1	√	√	...	...	...	...	84	130/70	+2	0	..	..	Dimin.	Norm.	Achlor.	
7	Neg.	√	√	√	√	√	√	√	√	...	...	...	...	72	145/80	+2	0	..	..	Dimin.	Norm.	Achlor.	
8	+3	+32	+22	+12	0	+4	+2	√	√	118	...	210	178	76	122/70	+2	+	..	..	...	...	Hypo.	Norm.
9	Neg.	+16	+24	+34	0	0	Norm.	√	√	...	...	...	...	72	108/74	√	0	..	..	...	Norm.		
10	+3	+ 5	+ 3	Same	0	0	Absent	√	√	103	...	169	128	63	120/69	+3	+	..	..	...	...	Hypo.	
11	Neg.	+ 8	+12	+28	0	0	Norm.	√	√	...	...	...	...	98	110/78	+2	0	..	..	Absent	...	...	Delay.
12	Neg.	0	−20	Same	0	0	Absent	√	√	...	...	...	...	72	120/60	+1	0	..	..	Absent	Hyper.	Norm.	Norm.
13	+2	+22	+23	+48	0	0	Norm.	√	√	...	...	...	...	78	121/79	±	0	..	+	Absent	Dry	Norm.	
14	√	+32	0	+14	0	0	Dimin.	√	√	...	...	...	...	76	110/74	±	0	..	+	Absent	Norm.	Norm.	
15	+3	−16	+12	+26	0	0	Dimin.	√	−14	...	...	...	...	112	108/64	+2	0	..	+	+	Hyper.	....	Norm.
16	+1	+ 8	+ 4	+20	0	0	Dimin.	√	√	...	...	...	...	58	128/76	+2	0	..	+	...	Hyper.	Hyper.	Norm.
17	Neg.	+ 5	−12	Same	+1	+1	Dimin.	Neg.	+5	87	151	131	115	100	132/80	+2	+	..	+	...	Dry	Hypo.	Norm.
18	+4	+14	+18	+12	0	+3	+1	√	√	89	153	157	109	96	100/54	+3	0	..	+	...	Dry	Hypo.	Norm.
19	+4	+ 7	+22	+24	0	0	Norm.	√	√	96	148	130	113	80	110/40	√	+	..		...			
20	+4	√	√	√	√	√	√	Neg.	+16	...	...	...	...	100	....	+2	0	+	..	Norm.	Hyper.	Hypo.	Delay.
21	+3	√	√	√	√	√	√	√	√	...	...	...	...	...	....	+4	0	..	..	...	...	Hyper.	Norm.
22	+3	+ 4	−10	+ 4	0	+1	Dimin.	Neg.	√	87	166	178	101	72	130/80	0	0	+	..	...	Dry	Norm.	Norm.
23	Neg.	+10	+24	+24	0	0	Norm.	Neg.	+3	90	140	155	135	68	112/84	0	0	+	..	Norm.	Hyper.	Hypo.	Norm.
24	+3	+24	+32	+32	±	+4	+2	+1	√	91	160	157	122	94	138/100	+2	+	+	..	...	...	Hyper.	Norm.
25	Neg.	+ 8	+20	+30	0	+1	Norm.	√	√	82	120	100	107	78	120/80	+2	0	..	..	...	...	Hyper.	Norm.
26	+3	+12	+25	+30	0	0	Norm.	+1	+38(?)	100	98	126	89	84	120/80	+1	0	..	+	...	Hyper.		
27	+1	+10	+54	+34	0	+4	+3	√	√	96	126	166	157	68	110/70	√	+	..	..	...	...	Norm.	Norm.
28	+1	+ 6	+30	+40	0	+1	+1	Neg.	+10	93	142	122	100	68	120/80	0	0	..	+	Hyper.	Dry	Norm.	Norm.
29	+4	+ 6	+10	+ 6	0	0	Norm.	√	√	...	...	...	...	82	108/74	√	0	..	..	...	...	Hypo.	Norm.
30	+4	+32	+30	+40	0	+2	+1	√	+10	104	190	221	217	78	110/90	√	0	..	..	...	...	Hypo.	Delay.
31	+1	+18	+18	+34	0	0	Norm.	√	√	89	122	100	87	80	142/100	√	0	..	..	...	...	vpo.	Norm.
32	+2	+18	+20	+24	0	0	Norm.	√	√	100	133	157	130	72	110/80	+1	+	..	+	Absent	Hyper.	Hyper.	Hyper.
33	+1	+16	+20	+30	0	0	Norm.	Neg.	√	100	143	137	120	80	150/100	+2	0	+	..	√	...	Norm.	Norm.
34	√	+ 4	+ 4	+10	0	0	Dimin.	√	−16	...	...	...	...	76	112/66	+4	+	..	+	Absent	...	Hypo.	Norm.

Widal Hemoclastic Crisis: A postprandial drop in the number of white cells of less than 500, + 1; a drop of from 500 to 1000 cells, + 2; a drop of from 1000 to 2000 cells, + 3; a drop of more than 2000 cells, + 4.

Goetsch Test: The maximum rise (+) or fall (−) in pulse rate after adrenalin is recorded in column 3. The maximum rise (+) or fall (−) in systolic blood pressure after adrenalin is recorded in column 4. The maximum increase (+) or decrease (−) in pulse pressure after adrenalin is recorded in column 5.

The occurrence of glycosuria in urine examined three hours after adrenalin injection is recorded as + and its absence as 0 in column 6. √ Test not performed. In column 7, the constitutional reaction is graded as absent (0) or +1, +2, +3, or +4 depending upon the presence and degree of tremor, nervousness, vertigo faintness, syncope, etc. In column 8, all factors are taken into consideration in classifying patient as having a positive (+ or hypersensitive), normal, diminished or absent response to adrenalin. The occurrence of mydriasis after introduction of adrenalin into the eye is recorded as + (positive) and its absence as neg. (negative) in column 9.

Basal Metabolic Rate is recorded in column 10, and ordinary glucose-tolerance test in column 11. The pulse rate and systolic and diastolic blood pressure are recorded in columns 12 and 13 respectively.

Dermographism is graded into absent (0), +1, +2, +3 and +4, depending upon the intensity of the reaction. A history of urticaria is marked +, its absence 0. Columns 16 to 21 inclusive are self explanatory.

Eppinger and Hess consider an excessive reaction to adrenalin an indication of sympathicotonia. One-half cubic centimeter of adrenaline chlorid (1 to 1000) was injected intramuscularly and five-minute observations were made of the pulse rate and blood pressure. The urine was tested for sugar one and two hours after injection. The usual criteria were accepted as indicative of a positive response, that is, rise in systolic blood pressure and pulse rate of 30 or more. The degree of constitutional reaction as manifested by tremor, nervousness, faintness, vertigo, syncope, and so forth, was also taken into consideration in grading the result. Thirty-one cases were tested. There was an absence of positive reaction in 19 cases (61 per cent). Glycosuria occurred in 2 cases following the injection.

Sugar Tolerance. Eppinger and Hess claim an increased carbohydrate tolerance in vagotonia. Seale Harris[26] described finding reactions similar to those resulting from an overdosage of insulin in patients who had not received insulin. He called this condition hyperinsulinism. Nielsen[27] records the presence of a similar reaction which he terms "hypoglycemic" in 15 of 17 cases of "generalized vagotonia" during the course of a glucose-tolerance test. The reactions may not be severe according to Nielsen, in some cases merely consisting of profuse perspiration and weakness. In 16 of our cases of neurogenic mucous colitis, there was not a single occurrence of hypoglycemia at any time following the ingestion of glucose (Table I). Our tests were only continued for a period of two and a half hours. Since some of Nielsen's cases had a hypoglycemic tendency at two hours and many of them had a rather definite subnormal figure at three hours, we feel that a tendency toward hypoglycemia should have existed at two and a half hours if it were going to be present. In cases Nos. 8 and 30 diabetic curves were obtained. These cases were both grave, long-standing vegetative imbalance types which exhibited vagotonic tendencies but are really mixed types of vegetative disturbance. In cases 10, 23, 24, 27 and 32, all patients with clinical leanings toward so-called vagotonia there is slight evidence of decreased sugar tolerance, all of them exhibiting a slow return to normal after the ingestion of sugar.

Basal Metabolism. Ten cases were tested. Two cases were on the borderline of decreased metabolism, −14 and −16. Both had most of the signs of parasympathetic preponderance. The remaining cases tested were within normal range except one with a metabolism of +16. The marked tendency toward lessened basal metabolic rate which Nielsen reported in vagotonia was not present in our cases, although their number is too small to be of much value.

The Adrenalin Mydriasis Test of Loewi. Introduced as a test for pancreatic disease, but has been considered by many as an indication of activity of the chromaffin and sympathetic nervous system when positive. Twelve patients were examined. Nine had negative reactions and 3 slightly positive.

Basal Metabolic Rate is recorded in column 10, and ordinary glucose-tolerance tests in columns 12 and 13 respectively.
Adrenalin test is recorded in column 11.
Columns 16 to 21, inclusive are self explanatory.
Absent (0), +1, +2, +3 and +4, depending upon the intensity of the reaction. A history of urticaria is marked +, its absence 0.

Summary of Influence of Vegetative Nervous System. A short synopsis of the studies made to determine the vegetative system function is given in Table II. The incidence of a history of urticaria, of oily tendency of the skin and appendages, dermographism, hypersalivation, hypotension, sphincteric spasm, colonospasm, positive Widal hemoclastic crisis, negative Goetsch test, and blunting of the pharyngeal reflex might be considered as suggestive of parasympathetic preponderance. The hyponormal acidity, mydriasis and the symptoms and signs of vasomotor instability could be attributed to sympathetic overactivity. By consulting Table I an idea may be had of the reactions on each patient. If we could

TABLE II.—SYNOPSIS OF FUNCTION OF VEGETATIVE NERVOUS SYSTEM.

Condition.	Percentage of cases positive.
1. History of urticaria	26
2. Oily hair	47
3. Oily skin; 4 times as frequent as dry, most cases normal	—
4. Dermographism	80
5. Evidence of vasomotor instability (subjective and objective)	Most cases.
6. Pupil: Myosis	29
Mydriasis	35
7. Pharyngeal reflex: Diminished or absent	42
Increased	26
8. Salivation: Hypersalivation	54
Hyposalivation	14
9. Pulse rate: Normal variations	—
10. Blood pressure: Hypotension	30
Slight hypertension	22
11. Leukopenia	Slight
12. Lymphocytosis	Slight
13. Eosinophilia	Absent
14. Gastric acidity: Hyponormal	30
Hyperacidity	24
15. Gastric motility: Delayed	30
16. Tendency toward sphincteric spasm	Increased
17. Colonospasm	43
18. Blood sugars	Normal
19. Decreased sugar tolerance: No hypoglycemic reaction	Tendency
20. Basal metabolic rate	Normal range
21. Adrenalin mydriasis test of Loewi: Positive	15
22. Widal hemoclastic crisis: Positive	77
23. Goetsch adrenalin test: Negative	61

accept the tests listed as physiologically sound, which we cannot, while the mechanism of their action is so little understood, the following classification of the 34 cases might be made. The reactions suggest parasympatheticotonia in 9 cases (Nos. 2, 3, 10, 15, 19, 20, 21, 26 and 29). In the remainder, a mixed picture is present. In no case are the clinical or laboratory criteria for pure sympathicotonia fulfilled. We cannot accept the terms vagotonia and sympathicotonia as indicative of definite, clear-cut types of imbalance, although our present knowledge may permit of a designation of vagotonic or sympathicotonic tendencies or coëxisting hyperexcit-

ability of both systems. In reaching this conclusion we are but reiterating the opinions of an increasing number of observers. The conception of vagotonia as distinctly opposed to sympathicotonia clinically has little clinical or experimental basis. A so-called vagotonic state does not exclude a coëxistence of sympathetic hyperexcitability. Petren and Thorling[28] have noted positive reactions both to pilocarpin and atropin in the same individuals. Lavastine[29] records hypersensitiveness to adrenalin and pilocarpin in the same patients. Dissociation of phenomena which occur in people sensitive to adrenalin or to pilocarpin has been noted by several. The same conclusion seems justified by our clinical findings. These cases show evidence of parasympathetic overactivity and in addition a majority had hypersensitiveness of the orthosympathetic mechanism. We would conclude that in neurogenic mucous colitis there is an underlying basic instability of the vegetative nervous system, involving in most instances overactivity of both the parasympathetics and the sympathetics, the former picture being the more pronounced. Since there is no evidence of inflammation of the colon to provoke an overproduction of mucus as in ulcerative colitis, we believe the ever-present neurogenic disturbance is the important etiologic factor.

Allergy. Gastrointestinal symptoms have been attributed to allergic reactions resulting from the ingestion of certain foodstuffs by Duke[30] and by Adresen[31] and others. Hollander[32] has recently reported 5 cases of mucous colitis due to food allergy. Seventeen cases were subjected to food sensitization tests, using both the intradermal and scratch methods. Eight patients were negative to all foods. In 9 cases, there was slight reaction to one or more foodstuffs. None of the reactions was graded beyond a +1. One patient developed diarrhea after eating onion. She was sensitive to onion by skin test. A second patient with diarrhea was found to be sensitive to certain fish, cheese and nuts. Eliminating them from the diet caused a disappearance of the diarrhea. In the remaining cases, there seemed to be no relationship between the ingestion of the food in question and the production of symptoms. Allergy does not appear to be of great importance in the etiology of neurogenic mucous colitis.

Effect of Calcium and Parathyroid Extract. Although we do not intend to discuss therapy of neurogenic mucous colitis, we wish to report our experience with calcium because of its possible bearing on the etiology. Calcium has been recommended for many years in various apparently dissimilar conditions which upon analysis seem to have a common background of vegetative nerve imbalance. While the knowledge of calcium metabolism is still imperfect and its use is often empirical, the investigations of many workers in different phases of calcium metabolism have been applied therapeutically. The recent contribution of Collip[34] and of others on the

importance of parathyroid hormone as a regulator of calcium metabolism has led to a wider acceptance of parathyroid extract as a valuable adjunct in determining calcium effect. Large and frequent doses of calcium combined with parathyroid extract have been used with some benefit in urticaria, hay fever, vasomotor coryza, certain forms of eczema, migraine and even asthma. (Cohen and Githens.)[33] The work of many investigators in this field indicate that the beneficial effect of calcium in conjunction with parathyroid is due to lessened cell permeability thus diminishing transudation, improvement in the vegetative nerve function possibly by decreasing the hyperexcitability of the parasympathetic system and relief of smooth muscle spasm.

TABLE III.—RESULTS OF THERAPY.*

Case.	Therapy.	Time in weeks.	Local symptoms.	Nervous state.	Sigmoidoscopic picture.	Mucus.
1	C. P. 5	4	Relief diarrhea and pain	Marked improvement	....	Less.
5	C. P. 6	4	No change	Same	....	Same.
9	C. P. 10	8	No change	Same	Normal	Same.
10	C. P. 15	8	Free from crisis; blood pressure reduced	Same	Same	Less.
11	C. P. 10	8	No change	Marked improvement	Same	
13	C. P. 10	8	Crisis less frequent and severe	Marked improvement	Improved	
Cam.	C. P.	12	No change	Psycho-neurotic, same	Same	Same.
16	C. P. 10	7	Relief tenesmus, diarrhea	.....	Improved	Less.
17	C. P.	8	Frequent dyspepsia; bearing down	Improved	Normal	Same.
18	C. P. 10	8	Crisis less frequent and severe	Improved	Improved	Less.
20	C. P. 6	5	Improved constipation	.....	Same	Less.
22	C. P. 12	7	Constipation better, otherwise same	Psycho-neurotic; no change	Same	Same.
23	C. P. 12	5	No change	Same	Same	Same.
25	C. P. 4	8	Relief constipation; cramps	.....	Normal	None.
26	C. P. 8	4	Improved constipation	Same	Same	None.
32	C. P. 3	3	Improved diarrhea	.....	....	Same.
J. E.	C. (vein) P. 3	2	Improved dyspepsia; constipation			
6	C.	8	No change	Same	....	Same.
8	C.	3	Exaggerated	Worse		
MacC.	C.	6	Improved constipation, dyspepsia	Marked improvement	Normal	Less.
30	C.	4	Same	Same	....	Less.
28	Ephed.	3	Improved	Improved	Normal	None.
33	Ephed.	2	Same	Same	Same	

* Case numbers correspond to cases of same number on Table I. C., calcium lactate. P., parathormone (Collip). The number following P. represents number of injections given. The sigmoidoscopic picture of these patients before therapy was typical of the condition as previously described.

Seventeen patients received combined calcium and parathyroid therapy (Table III). The calcium was given in the form of the

lactate, 30 gr. or more three times daily. Fifteen units of parathormone (Collip) was injected intramuscularly every third or fourth day. Relief from or improvement in the local symptoms was claimed by 12 patients. This was manifested by improvement in constipation in 4 cases, relief from constipation and cramps in 1 case, improvement in diarrhea in 1 case and complete relief from diarrhea and pain in 1 instance and from diarrhea and tenesmus in another. The mucus crises became less frequent and less severe in 2 cases. Relief from dyspepsia and a bearing down sensation occurred in 1 case. In a few cases, a striking change in subjective nervous phenomena occurred which seemed to be due to therapy. Several patients expressed themselves as feeling better in this respect than they had felt for years. Marked improvement occurred in 3 cases and moderate improvement in 2 cases. The nervous symptoms remained unchanged in 7 cases. Three of the latter were profound "neuropaths."

In 13 cases, the sigmoidoscopic examination was repeated after the use of calcium and parathyroid extract. The typical glairy, lustrous appearance had disappeared in 3 cases and was less marked in 2 cases. In 7 cases no change was noted. We hesitate to base evidence of improvement upon a change in the sigmoidoscopic picture, as the typical finding previously described has been noted to disappear and reappear in other patients who were untreated. A record was made of the amount of mucus discharged in 14 cases after treatment. No mucus was present in 2 cases and in 5 cases there was a diminution in the amount (patient's opinion). In 7 cases, no change was noted. There is naturally so much variation from day to day that the significance of the reduction in mucus is open to some question.

Four patients received calcium by mouth without parathyroid extract. In 1 case the condition was unchanged as was the sigmoidoscopic picture. In Case 8 local and nervous symptoms became worse. Case 30 remained the same except for a reduction in the amount of mucus expelled. Case MacC. experienced distinct improvement in her dyspepsia and constipation. She had an achlorhydria so that the result was not due to alkali. From a nervous standpoint she stated she felt better than she had for years. There was less mucus discharge from the bowel and the mucosa of the rectum and sigmoid lost its glairy appearance.

The combined use of calcium by mouth and parathyroid gland intramuscularly was accompanied by considerable subjective and questionable objective improvement in most cases upon which it was tried. An insufficient time has elapsed to evaluate it properly. Judging from experience with calcium alone on a much smaller group, its therapeutic value is enhanced by combining it with parathyroid gland.

Summary. The prevalence, obscure pathogenesis and frequent failure to diagnose neurogenic mucous colitis lead us to analyze 50 cases of this condition.

1. We feel that it is possible to make a diagnosis of the condition or at least to suspect its presence by sigmoidoscopic examination alone in many atypical cases. A picture which seems almost pathognomonic is described. This examination is of paramount importance in patients with local bowel disorders who show evidence of vegetative nervous system instability.

2. The gross and microscopic appearance of the mucus, which can best be obtained through the sigmoidoscope, is also characteristic. There is little justification either from sigmoidoscopy or the character of the mucus discharge for attributing this condition to inflammation of the colon.

3. Eight patients of the 50 were probably unnecessarily subjected to laparotomy, reëmphasizing the importance of considering mucous colitis as a cause of periodic abdominal pain.

4. So-called mucous colic was present in a minority of cases. Pseudomembranous mucus was encountered in a very small percentage. Colic attacks are not dependent upon the formation or expulsion of membranes. The name mucomembranous colitis had better be discarded, as it does not include the majority of cases in which membranes are not passed, but which are identical with the membranous cases in all other respects. The most common situation of the pain is in the lower left quadrant. Many of our cases did not complain of pain. Although we are in accord with the emphasis placed upon constipation as an associated condition, we doubt its importance as an etiologic factor and would attribute its presence to the same underlying cause which is responsible for the mucous colitis. Twenty-four per cent of our cases had no evidence of constipation. Dyspeptic symptoms were encountered in the majority of patients. The stress placed upon the nervous factor by all authors is justifiable, but the classification of the nervous disorders frequently accredited to these patients is at fault. They are often of a hypersensitive, "impressionalistic" nature. The most common nervous symptoms encountered were emotional instability, depression, exhaustion and introspection. Less than half were neurasthenic and very few had definite psychoneuroses.

5. Slightly more than half of the patients were splanchnoptotic and of asthenic habitus. Colon tenderness was present in 66 per cent of cases, being more common over the left colon.

6. Because of a reputed association between dysfunction of the vegetative nervous system and mucus discharge from the bowel, an especial attempt was made to investigate this relationship. This analysis was based upon data from the clinical histories, relative symptoms and physical findings, the usual laboratory examinations which might throw an incidental light upon vegetative function

and, in addition, certain special tests which are considered to reveal abnormalities of this system. A short summary of the results of this study will be seen in Table II. It is our belief that the etiology of mucous colitis is in some way linked to the alterations in function of the vegetative nervous system. We do not subscribe to the terms vagotonia or sympathicotonia as indicating clear-cut and opposed entities, as most of our cases revealed evidence of overactivity of both systems. Symptoms and signs attributed to stimulation of the extended vagus mechanism are more obvious and probably of more importance.

7. Allergy played an insignificant, if any part, in the etiology.

8. The results of the use of calcium combined with parathyroid gland are recorded in some cases.

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INTRAPLEURAL PRESSURES IN MASSIVE COLLAPSE OF THE LUNG.*

With Report of Cases.

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Massive collapse of the lung, or more properly, massive atelectasis, has been reported as occurring:

(*a*) In obstruction of the bronchus from within: foreign body, intrabronchial tumor, mucus plugs, excessive secretions.

(*b*) In obstruction of the bronchus from without: pressure of aneurism, mediastinal tumor, pericardial effusion.

(*c*) In obstruction of the bronchus by chronic inflammatory pulmonary disease: tuberculosis.

(*d*) As a complication of trauma, or operative procedures.

(*e*) As a complication of severe infections grossly involving the nervous system, reported in postdiphtheritic paralysis, acute meningitis, and acute poliomyelitis.

A review of the literature reveals a multiplicity of theories regarding the cause of massive collapse or atelectasis. Immobility of the patient, and his position in bed, following trauma and operation, resulting in deficient expansion and aëration of the bases of the lungs, and an accumulation of bronchial secretions, are looked upon as the causative factors by some authors. A reflex nervous origin of collapse occurring as a posttraumatic and postoperative complication is the basis of various theories:

1. Vasomotor, with dilatation of vessels and stasis, producing bronchial obstruction by outpouring of secretions.

2. As being inhibition or paralysis of the bronchodilator fibers of the vagus, with overactivity of the bronchoconstrictors.

3. As being reflex paralysis of the diaphragm, either alone, or associated with excessive secretions.

Bronchial obstruction, irrespective of the type or character of the obstructing agent, remains the only definitely proven constant factor. Bartels (1860), first suggested absorption of alveolar air by the blood as a factor in collapse. Lichtheim's two series of experiments on rabbits, the first in which plugging of the bronchus resulted in pulmonary collapse, and the second, in which plugging of the bronchus, and ligation of the vessels to the obstructed lung failed to result in collapse, proved that it occurred as a result of the

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absorption of the entrapped alveolar air by the circulating blood. The recently reported exhaustive experiments of Coryllos and Birnbaum completely confirm this fact, and further stress the necessity of complete bronchial obstruction to the production of collapse.

Irrespective of the causative factors, the physical findings are constant:

1. Retraction and immobility of the chest wall of the affected side.
2. A high fixed diaphragm on the affected side.
3. Dullness on percussion over atelectatic lung.
4. Breath sounds either tubular or absent.
5. Marked cardiac displacement toward the side of the lesion.
6. Roentgen ray findings of marked opacity of the lung, a high diaphragm, and typical cardiac displacement.

The basis of the symptomatology and of the typical cardiac displacement is also the subject of some theory; a decrease in available alveolar space due to collapse of a lung, and the extreme cardiac displacement have been suggested as being responsible for cyanosis and dyspnea; while change in intrathoracic pressures, either on the involved, contralateral, or on both sides, has been suggested as being the factor underlying cardiac displacement. Elliott and Dingley made mention of this possibility in 1914, and stated that "it is conceivable that intrapleural injections of oxygen, in order to restore balance of volume and push back the displaced heart and lung, might relieve the worst cases of cyanosis and dyspnea."

Following an experience with a case of posttraumatic massive collapse in 1921, we have felt that a study of the intrapleural pressures in these cases might give an adequate explanation for the symptoms and the physical phenomena exhibited. As reported by Dr. Gordon Wilson, in discussion before the American Climatological and Clinical Association in 1927, we had had the opportunity, some years previously, of observing the marked increase in intrapleural, negative pressure existing in massive collapse, and subsequent observations in additional cases have led us to look upon these pressure changes as not only characteristic of collapse or atelectasis, but also as being responsible for the characteristic findings.

Based on our experience with artificial pneumothorax, we have considered an intrapleural negative pressure varying with respiration between −40 and −70 mm. of water as being the average normal. These figures closely coincide with those of Aron, who found in 36 normal individuals, an average negative intrapleural pressure varying with the phases of respiration between 2.54 and 5.9 mm. of mercury, corresponding to 34.29 and 79.6 mm. of water.

It is evident that in a normal individual, pulmonary expansion, and the normal relationship of the thoracic organs are maintained by atmospheric pressure exerted intrapulmonarily *via* the trachea, and by this negative pressure or suction equally exerted in both pleuræ. A release of this suction by the entrance of air or fluid into the pleura

is followed by true collapse of the lung, which, though its elasticity and recoil, contracts away from the chest wall, the negative pressure falling, or becoming positive. The term collapse, as applied to massive collapse or atelectasis, is misleading, as separation of the lung from the chest wall is not demonstrable. On the contrary, contraction in the lung tissue occurs toward the chest wall of the affected side. As suggested by Coryllos and Birnbaum, the term apneumatosis would appear preferable. In this condition, collapse, atelectasis, or apneumatosis, occurs without the entrance of air into the pleura. Fluid of insignificant amount, however, has occurred in several reported cases. The suction or negative pressure normally existing in the pleura is markedly increased, and displacement of the heart, mediastinum and diaphragm results, the structures being drawn toward the affected side. In the literature, Farris records the intrapleural suction in 1 case varying with respiration between −100 and −160 mm. of water. Elkins reports the pressures measured in 3 cases, the highest varying between −12 and −15 mm. of mercury, corresponding to −162 and −202 mm. of water. These negative pressures are somewhat lower than we obtained in the 2 cases in which accurate readings were made, and there is a great probability that this suction will vary directly with the degree of atelectasis or collapse present in individual cases, accounting for the difference in degree of symptoms and cardiac displacement reported. So great may this suction be, in one of our cases varying between −25 and −32 mm. of mercury, or 337 and 432 mm. of water, that cyanosis and dyspnea develop, we believe, because of extreme cardiac displacement and acute overdistention or emphysema of the contralateral lung. A vicious circle is now established—bronchial obstruction, absorption of alveolar air, collapse of the lung tissue, marked increase in intrapleural negative pressure, which in turn can only draw the obstructing medium more firmly and deeply into the bronchus. It was on this basis that Wilson suggested that partial pneumothorax, by lessening this negative pressure, or converting it into a positive one, might be of assistance in forcing out the obstructing agent. In the literature, Farris reports 2 cases given immediate symptomatic relief by this means, and in 1 case to be reported here, the disappearance of a cyanosis and dyspnea immediately followed the injection of 600 cc. of air into the pleura.

Report of Cases. Four cases of massive atelectasis are to be reported, due to four different etiologic factors, with observations on the intrapleural pressures in each.

Case I.—In October, 1921, I had the opportunity of seeing with Dr. H. N. Foster, a patient, who following a crushing injury to the thighs and pelvis, was exhibiting symptoms of marked respiratory distress. Cough was slight, but cyanosis and dyspnea were extreme. Examination of the chest revealed no evidence of trauma. The physical signs elicited in the lungs were unlike anything we had previously encountered. The right chest

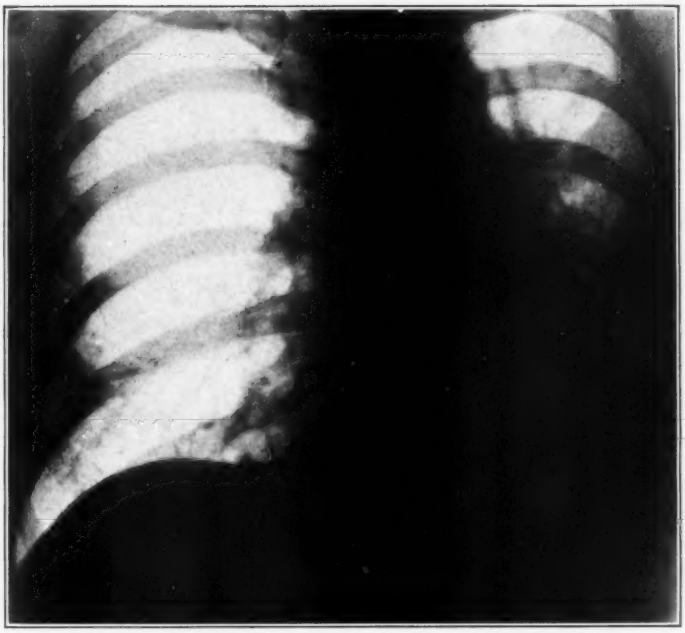

FIG. 1.—Case III. Roentgen ray March 8, showing partial collapse of left lower lobe.

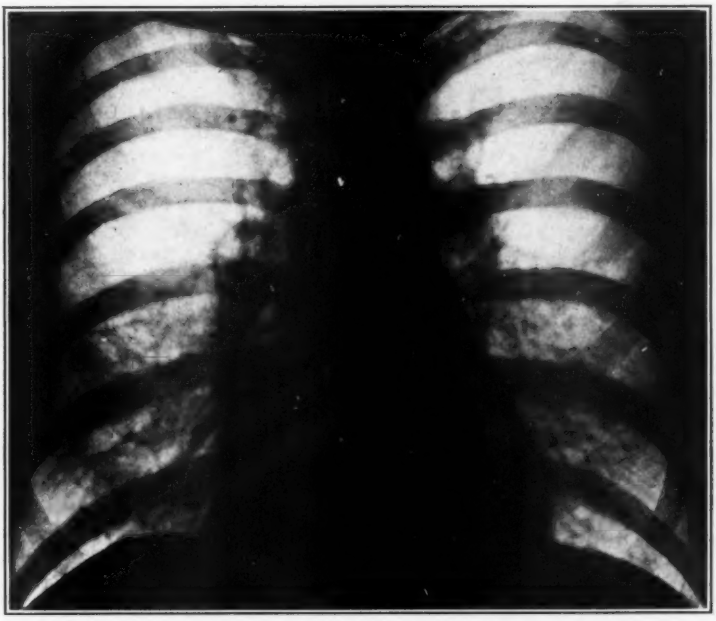

FIG. 2.—Case III. Roentgen ray March 29, showing lung completely expanded.

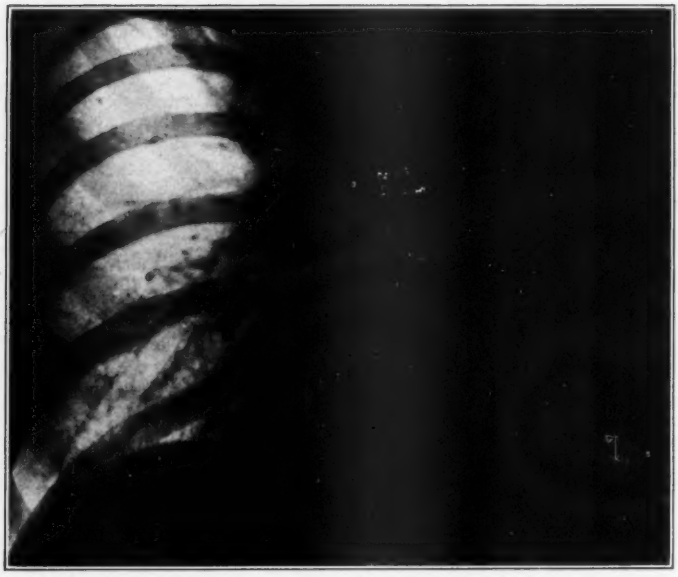

FIG. 3.—Case III. Roentgen ray May 5, showing recurrence of collapse of left lung.

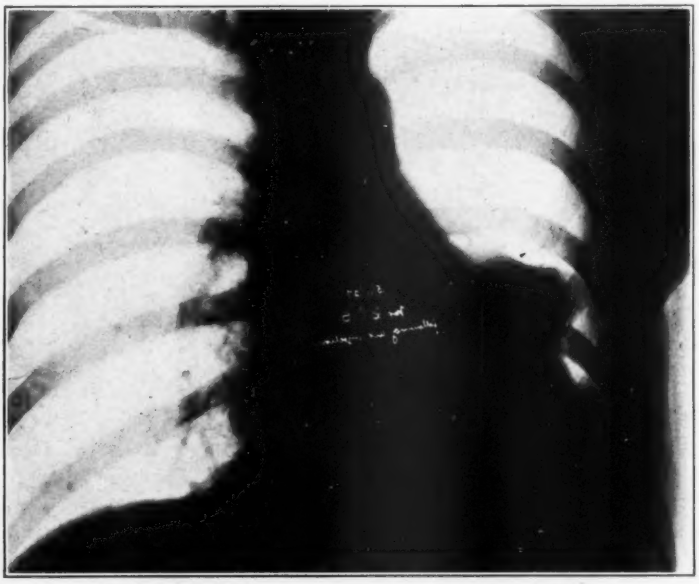

FIG. 4.—Case III. Roentgen ray May 11, showing partial pneumothorax, resulting from injection of 600 cc. air, which returned heart to practically normal position, and immediately relieved dyspnea and cyanosis.

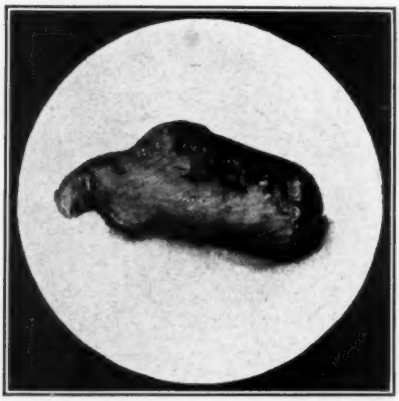

FIG. 5.—Case III. Cylindrical tumor mass coughed up by patient, measuring 4 by 1.6 by 1.1 cm.

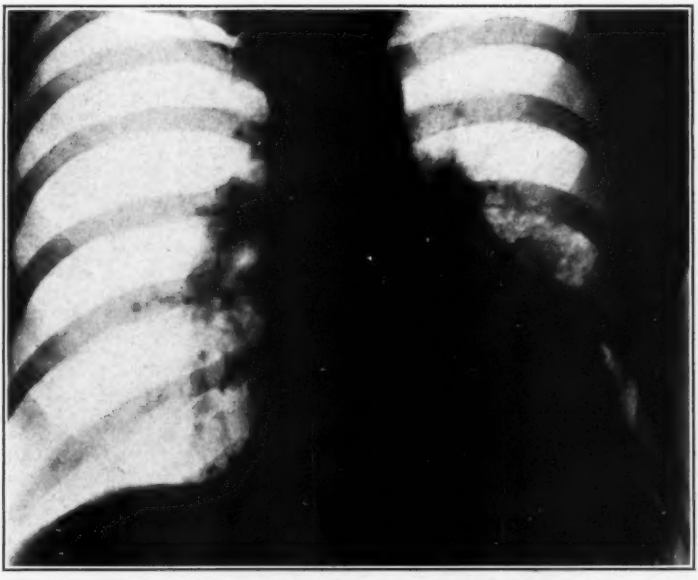

FIG. 6.—Case III. Roentgen ray showing expanding lung after coughing up obstructing tumor mass. Pneumothorax completely absorbed.

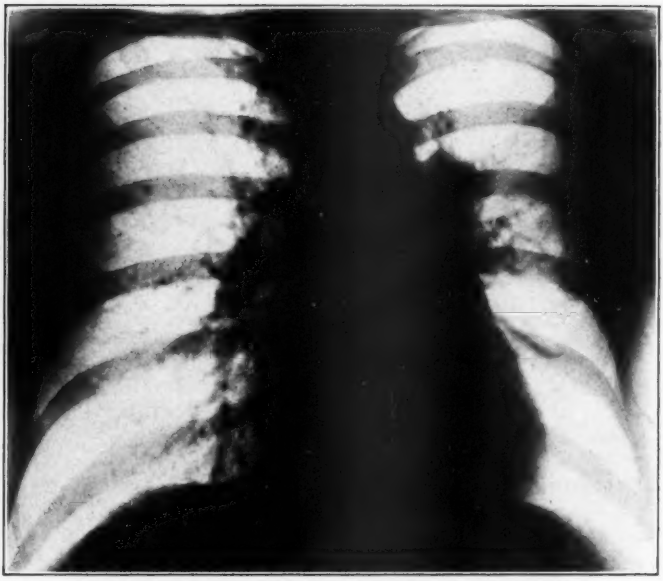

FIG. 7.—Case III. Complete expansion of lung.

FIG. 8.—Case III. Roentgen ray showing recurrence of collapse of left lung following attack of dyspnea and cyanosis September 12.

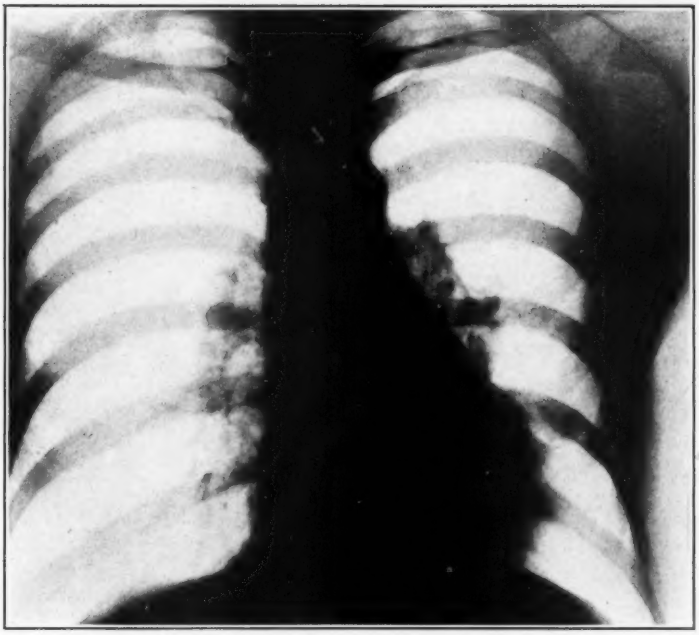

FIG. 9.—Case III. Roentgen ray showing complete expansion of lung following bronchoscopic removal of recurrent mass in left bronchus.

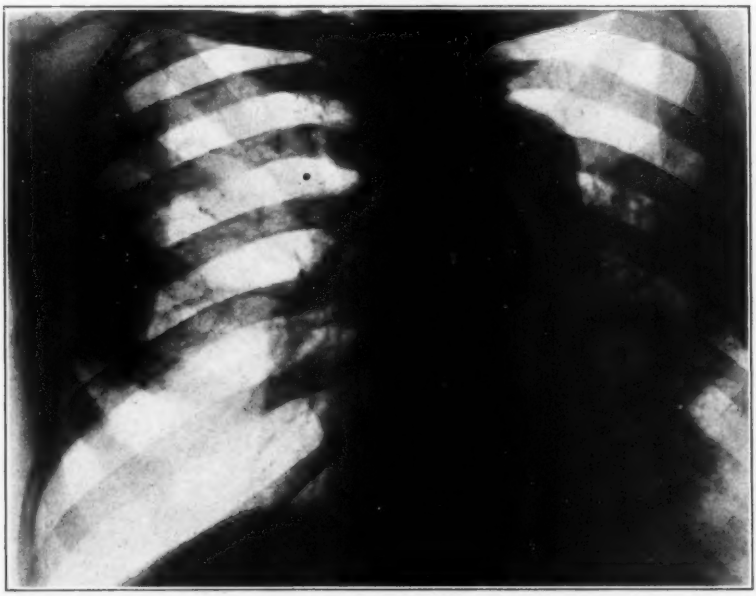

FIG. 10.—Case IV. Roentgen ray, January 22, 1928, showing opacity in left lower lobe, and a mediastinal mass, later shown to be aneurysm, and which rapidly obstructed left bronchus.

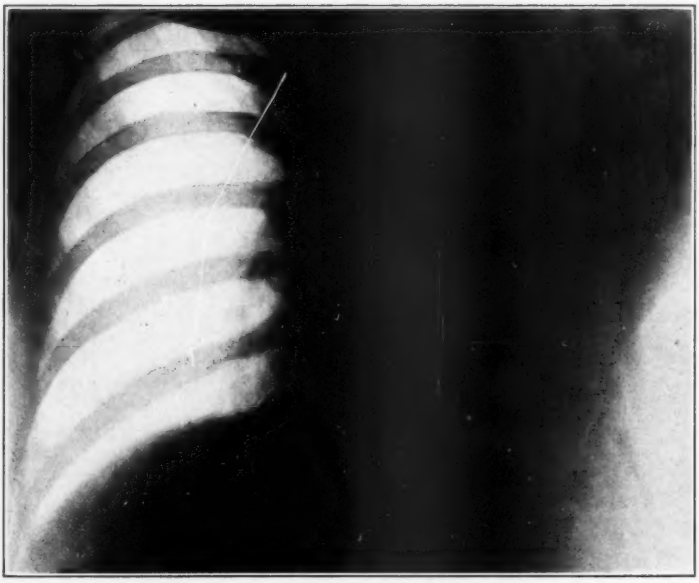

FIG. 11.—Case IV. Roentgen ray two weeks later. Complete collapse or atelectasis of left lung.

was full and showed wide respiratory excursions. The left chest was much retracted, flattened, and no respiratory movement was visible. The right lung revealed no abnormal signs. The left lung was resonant at the apex anteriorly, but from the third rib to base, and throughout the back, the percussion note was dull. Breath sounds were entirely absent. The heart was markedly displaced toward the left, the apex being in the fourth interspace, midaxillary line. The patient's condition precluded moving for Roentgen ray examination. Except for the cardiac displacement, the signs suggested fluid. A needle was introduced into the left pleura, but no fluid was obtained. A manometer was then attached, and to our surprise, the column of water was very violently and forcefully sucked into the pleura before the needle could be withdrawn. The manometer used was of 130 mm. in height, ample, in our experience, for measuring intrapleural pressures. It was evident after some thought that collapse of the lung without the entrance of air into the pleura alone would account for this marked increase in negative pressure, as it must necessarily increase whatever vacuum already exists, just as we had seen long-standing cases of artificial pneumothorax, from whose pleura the injected air had been absorbed, and in whose lung expansion was impossible due to the marked fibroid change, exhibit extremely high negative pressures. Reference to a text revealed that the signs elicited in this case checked with those described in massive collapse of the lung. It seemed reasonable then, that this suction might be a characteristic finding in pulmonary collapse. The patient died within a few hours of the effects of his injury. No autopsy was performed.

Case II.—Mrs. A. R., an old case of tuberculosis, was admitted to the hospital complaining of dyspnea, which was out of all proportion to other symptoms present. She had developed tuberculosis four years previously, and had done well on treatment, gaining 40 pounds, until November, 1926, when there was a gradual onset of dyspnea. This symptom increased until time of admission to hospital. She was completely incapacitated and confined to bed. Examination revealed very minor signs at the right apex. The left chest was retracted and showed a marked decrease in movement. Percussion note resonant at the apex. From third rib to base and throughout the back, the note was dull. Breath sounds were distant, but had a distinctly tubular quality. The heart was displaced to the left. The impression was one of chronic tuberculous disease with displacement of the heart due to contraction of fibroid process. Roentgen ray showed marked opacity of the lung below the level of the second rib to base, with the heart drawn well over to the left. Roentgen diagnosis by Ashburn was massive collapse of lung. A needle was inserted into the left pleura and attached to a water manometer. Again marked increase in negative pressure was demonstrated, and only the immediate withdrawal of the needle prevented the fluid from entering the pleura. Pressure not accurately recorded, the manometer being of 120 mm. in height, and the pressure being considerably in excess of this. Partial artificial pneumothorax was then induced, dropping the pressure to within normal limits. A relief of symptoms was noted, and the heart appeared in normal position. Because of the improvement in symptoms, pneumothorax was carried on to completion, and has been maintained until the present, the patient being free from symptoms, and leading again a practically normal life for the first time since the onset of her original tuberculosis.

Case III.—G. C. S., white male, aged forty years, had been in excellent health until onset of present complaint, with the exception of a mild attack of influenza which lasted three days, during 1917. On New Year's night,

1927, he was attending a social function, when he had a sudden attack of coughing, and he believed at the time that he had aspirated a portion of a nut he was eating. There was slight hemoptysis, and he became alarmed and went home. An illness of three weeks' duration, diagnosed grippe, and characterized by fever, cough, and marked dyspnea followed. He returned to work February 1, apparently in his usual good health. On March 5, while running for a train, he had an attack of coughing which was followed in a short time by increasing dyspnea. Consultation was asked for during this attack which resulted in a diagnosis of tuberculosis, and the sputum was searched for bacilli on six occasions, with negative result. On March 8, Roentgen ray revealed opacity in the lower half of the left chest, with some cardiac displacement toward the affected side. Roentgen-ray diagnosis was one of chronic pulmonary disease, but three weeks later, a practically normal lung was disclosed by Roentgen ray. He resumed work, having no further difficulty until again following exertion on May 4, cough and dyspnea returned. At this time, cyanosis appeared, and the dyspnea was greater than formerly experienced. At this time, he came under the care of Dr. F. S. Orem, who very kindly asked me to see the patient with him. Examination revealed a well-developed and well-nourished individual. The temperature was slightly elevated, being 99.2° F.; pulse 72, of good volume and regular. Dyspnea was urgent, the patient breathing comfortably only when sitting up. The lips, ears and fingers were definitely cyanotic. The chest examination revealed a normal lung on the right. The left chest was markedly retracted and no respiratory excursion was evident. Again a resonant note was present above the third rib on the left, with the remainder of the left lung dull. Breath sounds were considerably diminished throughout, but over the entire lower lobe there was a distinctly tubular quality as evidenced by the whispered voice sounds. The heart was markedly displaced toward the left, the apex being in the third interspace, midaxillary line. There was an area of resonance between the heart and the sternum, where practically normal breath sounds were heard, being probably due to a portion of the contralateral lung which had followed the mediastinum in its shift.

Roentgen ray revealed marked opacity of the left lung, an elevated diaphragm, and marked cardiac displacement toward the side of the lesion. Roentgen ray diagnosis by Ashbury was massive collapse of the lung.

A needle, attached to an accurately calibrated mercury manometer, was inserted into the left pleura. A marked increase in negative pressure was present, the manometer readings varying with respiration between −16 and −20 mm., comparable to −246 and −270 mm. of water. Partial pneumothorax was now induced, 600 cc. of filtered air being introduced into the pleural cavity, dropping the pressure to −80 and −100 mm. The disappearance of cyanosis and dyspnea was almost immediate. Examination showed the heart much further toward the right. Symptoms very gradually returned during the next few days, as the injected air was absorbed, and two refills were done, reducing the pressure to a lower level each time. During the following week, a sudden attack of coughing was productive of fresh blood, and the patient coughed up a cylindrical mass which he very fortunately saved. This mass, a pedunculated tumor, measured 4 by 1.6 by 1.1 cm., on pathologic study being a cellular fibroma. Relief of symptoms was now complete, the physical signs clearing up, and Roentgen ray revealing a practically normal lung. He was bronchoscoped in the clinic of Chevalier Jackson, where the stump of the tumor was located in the left main bronchus, the stump was fulgurated. Pathologic report from Jackson's Clinic was of benign inflammatory tissue. No further symptoms developed until September 12, when dyspnea again returned, the signs and Roentgen ray evidence of atelectasis of the left lung reappearing. He

remained at home for some time, but was finally prevailed upon to submit to bronchoscopy, a recurrence of the mass in the left bronchus being found. He returned to Jackson's Clinic on March 3, 17, and 24, for removal of the mass, and on April 14, for further observation, the mass having been removed in the first three attempts. Expansion of the lung followed relief of the obstruction, Roentgen ray on April 18 revealing a well aërated lung.

CASE IV.—Colored male, aged thirty-two years, was admitted to hospital January 21, 1928, complaining of pain in the left chest which was rather sudden in onset. His past history was unimportant. He denied venereal diseases. The present illness dated from January 1, when cough developed, hoarseness and dyspnea appearing in a short time, the dyspnea being referable to exertion. One week prior to admission, slight hemoptysis occurred. On admission, examination showed temperature ranging from 100° to 103° F., the pulse averaging 120. The right lung was clear. The left lung showed a dull note over the lower lobe, with diminution of breath sounds and fine râles. Dyspnea at this time was not urgent, but the respiratory rate was increased, averaging 26 per minute.

Blood count showed a leukocytosis of 25,000, 85 per cent of which were polymorphonuclear cells. The sputum was negative for tubercle bacilli. Blood Wassermann 75 per cent positive. Roentgen ray showed opacity in the left lower lobe, suggesting pneumonic process, and an evident mass in the mediastinum above the heart area. The heart was somewhat toward the left. Under fluoroscope, much difference of opinion arose as to whether pulsations were or were not visible in this mass, with the consensus being that no pulsations occurred.

While in the hospital temperature continued, and dyspnea became progressively worse. The lung signs also progressed, until two weeks after admission percussion note was dull throughout the left side. The breath sounds were entirely absent. The heart became displaced more markedly toward the left side, and an area of resonance appeared between it and the sternum. A clinical diagnosis of atelectasis of the lung, due to pressure on bronchus was made. Roentgen ray revealed marked opacity of the left chest, with heart well out toward the left.

Bronchoscopic examination disclosed obstruction in the left main bronchus, 4 cm. below the bifurcation.

Because of Gwyn's suggestion that a study of the intrapleural pressure on the unaffected side might be of value, needles were inserted into both pleuræ at the same time, the one on the unaffected side being attached to a water manometer of 140 mm. in height, and the one on the involved side to an accurately calibrated mercury manometer. The negative pressure encountered on the unaffected pleura was within normal limits, there being a negative pressure varying between −40 and −80 mm. of water. Elkin's 3 cases also revealed little change in pressures on the uninvolved side. On the affected side a tremendous increase in intrapleural negative pressure was demonstrated, varying with respiration between −25 and −32 mm. of mercury, with a mean pressure of −28, comparable to −337 and −432 mm. of water. Two weeks later the patient had a sudden hemorrhage and died.

Autopsy. Anatomical diagnosis: Rupture of thoracic aneurysm into left bronchus. Atelectasis of left lung, with small areas of bronchopneumonia throughout. Small pulmonary abscess, left lower lobe.

Conclusions. 1. Four cases of atelectasis of the lung due to four different etiologic factors, are reported.

2. A marked increase in intrapleural negative pressure has been demonstrated in each.

3. High negative intrapleural pressures are constant accompaniments, and are characteristic of massive collapse. This pressure change is directly responsible for the physical findings of cardiac displacement, and is the factor underlying the symptoms of dyspnea and cyanosis.

4. Partial pneumothorax, reducing the negative pressure to within normal limits has given immediate symptomatic relief.

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MALTA FEVER: A REPORT OF FIVE CASES.

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and

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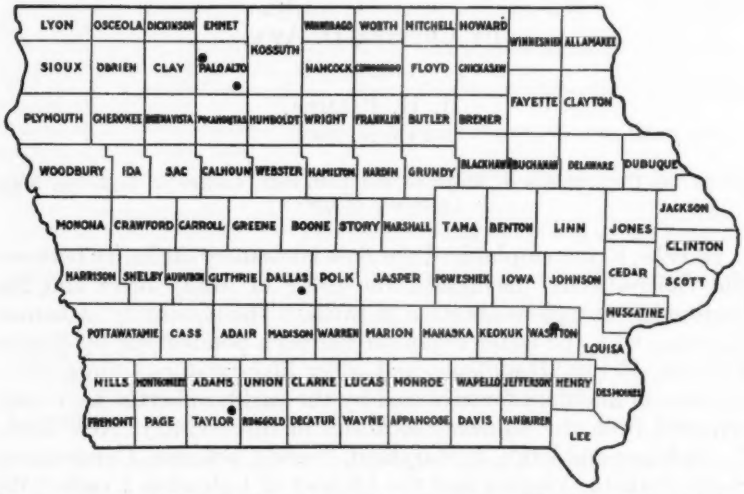
In 1918, Evans emphasized the close laboratory similarity between the "micrococcus" melitensis, the cause of Malta fever and the bacillus of contagious abortion in cattle. The possibility of human infection with the latter organism has been pointed out by Evans, Dickson, Bevan, Huddleson and other investigators. Since 1923, 20 cases of undulant fever caused by the bacillus abortus have been reported from the following localities in this country: New York, 7; Michigan and Utah, 3; Maryland, 2; and California, Connecticut, South Dakota, Virginia and the District of Columbia 1 each. We have recently had under observation 5 cases of undulant fever contracted in this State.

Case Reports Case I.—Mrs. A. L., aged thirty years, housewife, was admitted to the isolation service of the University Hospital June 9, 1927, as a typhoid fever suspect. She complained of weakness, fever of four weeks duration and diarrhea. About May 12, 1927, the patient began to tire easily and noted a dull ache beneath the scapulæ associated with slight shortness of breath. She continued to do her housework for a week, when her symptoms became more pronounced. She then consulted her physician who found a temperature of 102° with moist râles at the bases of both lungs. About May 23 she had a severe chill lasting for thirty minutes, followed by fever and a drenching sweat. She became so weak that it was necessary for her to remain in bed. The last week in May she had daily afternoon chills and sweats of gradually decreasing severity. Her temperature reached 106° during the first week in June. For ten days prior to admission, the patient was extremely nervous and according to relatives was delirious much of the time. She had diplopia, especially at night, and some photophobia. The appetite was poor. Her bowels were constipated, requiring

daily laxatives until June 5, when diarrhea developed with accompanying abdominal tenderness. There was an occasional nonproductive cough. The patient felt that she had lost about 10 pounds in weight. There were no joint symptoms.

Examination on June 9, revealed a listless, sallow-complexioned woman of thirty. The tongue was heavily coated. The lymph nodes were not palpable. The pulse was 100 per minute and not dicrotic. The blood pressure was 108 systolic and 70 diastolic. The lungs were clear except for a few sibilant and inconstant crepitant râles over the right upper front. The heart was of normal size. A soft systolic bruit was heard at the apex and at the pulmonic area. Inspection of the abdomen revealed several 2 to 4 mm. spots, resembling rose-spots, which faded on pressure. There was definite tenderness over the lower abdomen, particularly over the sigmoid. The liver was not felt but liver dullness seemed increased. The spleen extended 3 cm. below the costal margin and was soft and slightly tender.



The dots represent the localities from which Brucella melitensis, variety abortus, has been isolated from human cases.

During the first ten days of observation the daily afternoon temperature ranged from 103 to 105; the pulse from 100 to 110. The patient was listless, drowsy, and frequently complained of nausea and abdominal tenderness. There was one chill lasting for ten minutes. Excessive perspiration was a noticeable feature. There were two epistaxes. The diarrhea gradually subsided. The "rose spots," râles and cardiac murmur disappeared. A blood culture taken June 11, was positive for Brucella melitensis, variety abortus. The following week, the temperature declined to 102° each day. The only complaints were weakness and slight anorexia. On June 27, the fever rose to 103° and for the next six days it was about 104° each evening. On several occasions the patient complained of abdominal tenderness. Then followed a decline to below 101° for three days and a subsequent rise to between 102° and 103° from July 10 to 19. The patient was cheerful during this period and her appetite improved considerably. The temperature gradually subsided to reach 100° on July 23, when a blood culture was taken and on the following day 5 cc. of sterile milk were injected, causing a rise

to 105°. Two later injections of 10 cc. each were given July 28 and July 31, with resultant temperature increases to 103 and 104 accompanied by chills and severe headaches on each occasion. On August 2, the temperature was normal and the patient remained free from fever until her discharge from the hospital August 19, at which time she felt well except for slight weakness. The heart and lungs were negative and the spleen was not palpable.

Laboratory Data. The blood Wassermann test was negative.

The urine showed a trace of albumin on the first two examinations. Eight subsequent tests were negative. Many pus cells were found on several occasions.

On admission, the blood count showed 5,560,000 red corpuscles and 100 per cent hemoglobin. Between June 10 and 18, the white blood count on three occasions varied between 4500 and 10,250. There was an absolute mononucleosis. Malarial parasites were sought for but not found.

TABLE I.—BLOOD PICTURE OF CASE I.

Date.	Hemoglobin.	Red blood cells.	White blood cells.	Neutrophiles.	Normal lymphocytes.	Pathologic lymphocytes.	Large mononuclears.	Eosinophiles and basophiles.
June 28, 1927	80	4,940,000	6850	49.0	45.0	3	3	
July 7, 1927	..	4,700,000	5000	40.5	46.5	6	6	1
July 21, 1927	..	4,100,000	7200	41.0	45.0	12	2	
July 25, 1927	75	3,750,000	5300	61.0	24.0	7	5	3
July 28, 1927	75	4,180,000	6100	36.0	53.0	9	1	1

Bacteriologic and Serologic Studies. On June 11, blood was sent to the State Hygienic Laboratory for typhoid and Malta fever agglutination tests. These were reported negative. On June 16, the state laboratory reported a positive agglutination test for Malta fever. Positive tests were again reported on serum taken June 23, and June 25. The latter report was confirmed by the Hygienic Laboratory for the U.S.P.H.S. who found agglutination in dilution of 1 to 1280. Agglutination tests with Bacillus typhosis as antigen were negative throughout the course.

The first blood culture was taken June 11. About 3 cc. of blood were placed in a flask containing 100 cc. of dextrose meat infusion broth to which calcium carbonate had been added. After five days' incubation, the broth became clouded. It was subcultured on blood agar and examined after forty-eight hours' incubation. The slant was covered with minute round translucent colonies. Stained by Gram's method the organism was a minute Gram negative bacterium occurring singly, occasionally in pairs, and rarely in chains of three or four elements. It was nonmotile, grew on ordinary media and failed to ferment in carbohydrate media. It agglutinated in the patient's serum in dilution of 1 to 1280. It agglutinated in the same dilution in known serum for Brucella melitensis, variety abortus, obtained from the U.S.P.H.S. laboratory.

The patient's serum was absorbed with the organism obtained from her blood. Simple agglutination tests were then run on the absorbed serum, using Brucella melitensis in one series and Brucella melitensis, variety abortus (456) in another. The test was controlled with serum which had not been absorbed. Brucella melitensis was agglutinated by the absorbed serum in dilution of 1 to 160, while the known abortus variety failed to agglutinate. In the control serum each organism was agglutinated to and including dilutions of 1 to 1280. The patient's serum was then absorbed with Brucella melitensis, variety abortus (456). When simple agglutina-

tion tests were carried out on this absorbed serum, using Brucella melitensis and the patient's organism as antigens, it was found that the agglutinin for the patient's organism had been almost entirely removed, while Brucella melitensis agglutinated in dilution of 1 to 160. These reactions identify the organisms recovered from the patient as an abortus variety of Brucella melitensis.

Bacteriologic studies of the urine and feces were negative.

Guinea pigs inoculated subcutaneously with blood immediately after it was drawn from the patient's vein have remained symptomless to date.

On July 12, agglutination tests were run, using serum from each of the three cows which furnished the milk used by the patient prior to her illness. Cow No. 1 agglutinated in dilution of 1 to 40. The others were negative.

CASE II.—W. P., aged forty years, farmer, entered the hospital September 8, 1927. He complained of fever of five weeks' duration, weakness, and loss of weight. During the last week in July the patient felt feverish and tired. On July 31, he called a physician who told him his temperature was 104°. He was instructed to remain in bed and typhoid precautions were taken. The first two weeks in August his daily fever reached 104°. For four days beginning August 7 he had severe chills lasting about two hours, followed by drenching sweats. His only other complaint was intense morning headache. In the three weeks prior to admission, his afternoon temperature was 102° to 103°. The pulse increased from 80 to 100. He had one profuse epistaxis. About August 23, a mass was palpated in the right upper quadrant which later proved to be enlarged liver. His appetite was good, bowels were regular and there were no joint symptoms. There was a loss of 17 pounds in weight in five weeks.

On examination the patient showed evidence of moderate weight loss. The cheeks were flushed and complexion sallow. The heart and lungs were negative. The lymph glands were not enlarged. Pulse was 108 per minute and regular. The blood pressure was 112 systolic and 70 diastolic. There was a distinct fullness of the upper abdomen. The liver edge was felt a hand's-breadth below the costal margin. The spleen was 3 cm. below the left costal margin. The abdomen was not tender.

TABLE II.—BLOOD PICTURE OF CASE II.

Date.	Hemoglobin.	Red blood cells.	White blood cells.	Polymorphonuclears.	Normal lymphocytes.	Pathologic lymphocytes.	Large mononuclears.	Eosinophiles and basophiles.
Sept. 8, 1927	65	3,720,000	4000	38	18	30	14	
Sept. 18, 1927	70	4,980,000	3800	24	24	47	4	1
Sept. 27, 1927	60	3,610,000	2200					
Oct. 1, 1927	..	.....	3100	49	14	32	4	1
Oct. 1, 1927	..	.....	4800	60	20	17	3	
Oct. 2, 1927	..	.....	3900	50	24	21	5	
Oct. 2, 1927	..	.....	6300	63	21	14	2	
Oct. 4, 1927	..	.....	3100	49	18	29	3	1
Oct. 5, 1927	..	.....	3900	47	22	21	8	2
Oct. 10, 1927	67	3,980,000	3200	40	34	18	7	1
Oct. 15, 1927	..	.....	....	32	8	50	10	

During the period of observation, there were remarkably few symptoms. Excessive perspiration was noted frequently. There were several brisk epistaxes of from 200 to 500 cc., which were controlled by nasal packs. The fever was irregular with daily remissions, and lacked the undulant curve seen in the first case. On the 24th day of admission, the patient was given

an intramuscular injection of 5 cc. of sterile milk. The temperature increased from 102° to 104°. The following day the injection was repeated with a similar result. Blood counts taken two hours after treatment showed an absolute and relative polymorphonuclear increase. The fever gradually declined to normal within five days following the milk injections. The patient left the hospital in good condition on October 18.

Laboratory Data. Urine and stool examinations were negative.

The organism was recovered from the blood stream on three occasions. A positive agglutination test for Brucella melitensis, variety abortus, was obtained on the patient's serum. This was confirmed in the Hygienic Laboratory for the U.S.P.H.S.

The detailed laboratory study of this strain is not given because it does not differ from the A. L. organism.

CASE III.—Mrs. D. C., aged thirty-four years, a farmer's wife, was admitted to the University Hospital March 22, 1928. She complained of failing appetite and weakness during February. About March 10, she began to have high fever and definite shaking chills. She was delirious and semicomatose for two weeks prior to admission, during which time the temperature reached 105°. Blood serum sent to the State Hygienic Laboratory was reported to give a positive agglutination test for Malta fever. On entrance the patient was delirious, incontinent and muttering. Her cheeks were flushed, lips dry and tongue heavily coated. There were musical râles throughout both lungs and moist râles at the bases. The abdomen was diffusely tender and the spleen and liver were palpable. There was 65 per cent hemoglobin, 3,470,000 red blood cells, and 5600 white blood cells of which 42 per cent were mononuclears. From the blood culture taken March 23, an organism was recovered similar to those cultured from the other cases. For five days following admission, the temperature range was 102° to 105°. The fever then gradually subsided and the patient was discharged in good condition on the thirty-seventh day after admission.

CASE IV.—M. B., a farmer's wife, aged thirty-five years, entered the Hospital April 30, 1928. Weakness, tiredness and "loss of pep" characterized the first two weeks of her illness. During the third week, she developed fever, took to her bed, and was told by the family physician that she had the "flu." Fever and extreme weakness were her chief complaints of the fourth and fifth weeks. There were daily "spikes" of temperature, ranging from 101° to 105°, with intervals of one to three days of normal temperature. In the sixth week, the patient had several severe shaking chills. Drenching sweats, occurring particularly in the early morning hours, were prominent during the sixth and seventh weeks. On admission to the University Hospital, the patient did not appear severely ill. The temperature was 102.4°, pulse 100, and the spleen was palpable 4 cm. below the left costal margin. The hemoglobin was 60 per cent, red blood cells were 4,150,000, and white blood cells were 4800 of which 66 per cent were mononuclears. The first ten days of her stay in the hospital were characterized by daily "spikes" of temperature, ranging from 102° to 104.6°, profuse diaphoresis, weakness and poor appetite. On the fifth, seventh and ninth days milk injections were given. These were followed by marked improvement. The temperature during May ranged between 98.4° and 99.4°.

A positive agglutination test for Malta fever was reported by the State Hygienic Laboratory on blood serum taken during the second, third and seventh weeks. Blood taken during the eighth week of illness agglutinated Brucella melitensis, variety abortus, 1 to 320, and Brucella melitensis, variety abortus, was recovered from the blood culture taken at the same

time. One of the cows from which the patient obtained milk aborted during the past winter.

CASE V.—C. B., aged twenty-nine years, farmer, was seen April 19. He noted loss of appetite, increasing weakness and fever sometime prior to March 1. For three weeks prior to examination, he had been confined to bed with fever varying from 99° to 103.6°, accompanied by chills and profuse sweats. The latter were most common in the early morning hours. Nausea, anorexia and general weakness were persistent symptoms, and restlessness and insomnia had been prominent features. At times the patient was afebrile. At the time of examination he did not appear ill. The only positive finding was enlargement of the spleen. A differential blood count showed a mononucleosis of 46 per cent. The Widal reaction was negative. Blood culture taken April 19, was positive for Brucella melitensis, variety abortus, and the patient's blood serum agglutinated Brucella melitensis, variety abortus, and Brucella melitensis in dilution of 1 to 2560. The organism recovered agglutinated in specific serum in dilution of 1 to 5120.

Milk is supplied for the family by one cow. This cow has no history of infectious abortion, her blood serum does not agglutinate the patient's organism, and a milk culture is negative. In March, 1927, a cow which had an infectious abortion was sold. The patient is a breeder of thoroughbred hogs and spent much of his time caring for them. In January, 1928, he butchered five male hogs for home consumption. About the same time he sold several females because of sterility.

Comment. The clinical courses of the 5 cases are strikingly similar. A long continued irregular fever, frequent drenching sweats, leukopenia, mononucleosis, and an enlarged spleen in a patient who does not present a typhoidal state constitute the usual findings in Malta fever. To typhoid, malaria, and sepsis as causes for continued fever in a temperate climate we must add Brucella melitensis, variety abortus, infection. Even though the tentative diagnosis can be made from the above syndrome and agglutination tests, the positive blood culture is the only accurate method of diagnosing the disease. The relatively few complaints and the absence of complications is striking in all cases.

During convalescence we have an anemic, nervous individual who has lost 10 to 20 pounds in weight and 40 per cent of strength. The sudden termination of the temperature following intramuscular milk injections in 3 of our cases is remarkable. We must point out, however, that in each case the milk was given relatively late in the course of the disease.

The bacteriologic study presents several points of interest. In our first case, the agglutination test was negative a month after the onset of illness. This suggests the importance of repeated tests for a period of six weeks. We obtained organisms from the blood on every attempt as long as there was fever. It is to be noted that evidence of growth was absent until five days had elapsed.

In 3 of the cases, we feel that the source of infection was undoubtedly bovine; in 1 case the evidence was strongly suggestive of porcine infection, while in the remaining case no source could be traced.

It should be emphasized that the organism was recovered in each of our cases and that these cases came from widely separated localities as shown on the map. This indicates that infection with Brucella melitensis, variety abortus, in both man and domestic animals is prevalent throughout Iowa. Malta fever is undoubtedly more frequent than is indicated by this study and at the present time it is impossible to estimate the economic loss to the State from this disease.

Conclusions. 1. Brucella melitensis, variety abortus, has been isolated from the blood of 5 cases of Malta fever.

2. The clinical manifestations were similar with no important complications throughout the course.

3. The cases reported came from widely separated localities in Iowa.

4. A positive blood culture or high-titer agglutination test is necessary for the diagnosis.

5. A leukopenia and an absolute mononucleosis were present in all cases.

6. The 3 cases that received milk injections recovered promptly.

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A CLINICAL COMPARISON OF THE KOLMER MODIFICATION OF THE WASSERMANN TEST AND THE KAHN PRECIPITATION TEST IN SYPHILITIC AND NONSYPHILITIC CASES.

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Introductory. Recently, many workers have reported on the comparison of the Kahn and Wassermann tests giving the propor-

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tion of agreement between the two, based on thousands of tests, rather than the agreement of each test with the clinical findings. Our series of a comparatively small number of tests is presented as a study of both tests with respect to their agreement with each other and with the clinical findings. For this reason, we have divided the series into syphilitic and nonsyphilitic cases. Agreement between the two tests will vary with the frequency of repetition of the tests and the progress of the case under treatment. The syphilitic cases were further divided into various types in an effort to determine, if possible, which test was the more efficient in any special aspect of the disease, and moreover if the combined use of both tests led to the recognition of a greater number of syphilitic cases. The nonsyphilitic cases include miscellaneous dermatoses and patients who came for syphilitic investigation and were proved to be negative both clinically and serologically. Table III shows the various miscellaneous dermatoses studied and the percentage of agreement between the two tests.

The factors which we took into consideration in determining whether a patient had or had not syphilis were the physical examination; eye examination, medical consultation when indicated, repeated Wassermann (Kolmer modification) and Kahn tests of the blood; spinal-fluid examination; provocative procedure and family investigation.

The response of either the Wassermann or Kahn test to a recognized form of treatment is of importance but is not within the scope of this paper. Our percentage of agreement between Wassermann and Kahn judged by recent results presented by other authors is low. A bald statement of agreement, however, is not so much our aim as is the discussion of the clinical and serologic comparisons.

Historical. The Kahn precipitation procedure was first described in 1922[1] and has since been modified and improved. Keim and Kahn,[2] in a discussion of the Kahn and Kolmer methods in clinical practice, found the Kahn test more specific in all types of syphilis except in secondary syphilis where the two tests were of equal value. Very little mention is made of the dermatoses encountered in this survey. Greenbaum[3] tabulated two series of cases, one of syphilis with a positive Kolmer and a negative Kahn, and the other of syphilis with a negative Kolmer and a positive Kahn. He found that this latter type of disagreement occurred more often in treated than in untreated cases and that such disagreement argued for the use of the two tests together rather than either one alone.

Greenbaum and Yagle[4] found that 42 out of 50 patients presented daily uniformity in both tests (84 per cent) and that 8 showed a variation in tests done on twelve successive days. One or the other test was positive daily showing the importance of doing both tests. They conclude that if both tests are performed on a given serum the daily variation may be ignored. Becker[5] studied 69 patients

whose sera were anticomplementary to the Wassermann tests on 112 occasions. Of these 48 per cent were proved syphilitic and of the remaining nonsyphilitic 75 per cent were suffering from infectious diseases. He found no evidence that the substance which fixes complement with antigen also produces a positive precipitation reaction. He concludes, therefore, that the Kahn precipitation test is a valuable adjunct to the multiple procedure attack of Stokes[6] in the study of patients whose blood serum gives an anticomplementary reaction by the complement-fixation test. Other authors[7,8] have given only percentages of agreement in several thousand tests performed with no division of cases into syphilitic, or nonsyphilitic, and without regard to the stage of syphilis or to other dermatoses present.

Becker[9] found a total absolute agreement between Kolmer and Kahn tests of 69 per cent, total relative agreement of 10 per cent and total disagreement of 21 per cent in 2651 tests performed on 1776 patients. He found that there was difficulty in reading a weakly positive Kahn test, that the Kahn was reversed with greater difficulty by treatment, that it was more uniform in repeated examinations and that it exhibited a greater tendency to accentuation by treatment than did the Kolmer. He also emphasizes the fact that experience is necessary to correct reading of the test. Hopkins and Brunet,[10] in an article based on a questionnaire sent to serologists and as a review of previous agreement and disagreement findings, present in a concise and tabulated form the results of different workers throughout the country. With the exception of Becker,[9] the percentage agreement of other investigators has been higher than the one we now present.

Technique. The Kahn test was performed according to the technique outlined in Kahn's Manual;[11] the antigen was prepared in our laboratory and the titer varied from 1.1 to 1.3. The tests were shaken by hand. The readings were made independently* by three different observers both shortly after the test was completed and after being in the ice box overnight. The ice-box readings were employed in this tabulation. The entire afternoons of Wassermann days were given to the Kahn tests so that they were not hurriedly done. The first two tubes of the Kolmer method were used and the results repeatedly checked.†

Results. A total of 1702 tests were done on 631 cases. Of the 631 cases, 64 were investigations for the presence of syphilis which proved to be negative. Of the remainder, 351 patients had syphilis in some form and 216 had proved dermatoses without any evidence of syphilis.

The patients with syphilis were divided as follows: primary

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syphilis, 50 cases; secondary syphilis, 53 cases; late cutaneous syphilis, 11 cases; bone syphilis, 5 cases; cardiovascular syphilis, 25 cases; syphilis of the central nervous system, 83 cases; latent syphilis, 102 cases and prenatal syphilis, 22 cases. On these 351 cases, 1241 tests were performed by both the Kolmer and Kahn procedures.

The following table is based on the subdivision of these cases as above outlined and on the absolute and relative agreement, and on absolute disagreement between the Kolmer and Kahn results.

TABLE I.—SYPHILITIC CASES.

Type.	Tests.	Cases.	Absolute agreement.	Relative agreement.	No agreement.	Kolmer positive Kahn negative.	Kahn positive Kolmer negative.
Primary syphilis . . .	182	50	68.7	14.3	17.0	12.6	4.4
Secondary syphilis . .	184	53	54.3	29.4	16.3	10.8	5.4
Cutaneous late syphilis .	30	11	46.7	20.0	34.0	30.0	4.0
Bone syphilis* . . .	10	5	30.0	.....	70.0	60.0	10.0
Cardiovascular syphilis .	86	25	61.6	12.8	25.6	8.2	17.4
Neurosyphilis . . .	249	83	29.3	33.4	37.3	27.3	10.0
Prenatal syphilis . .	111	22	49.6	21.6	28.8	24.3	4.5
Latent syphilis . . .	389	102	45.8	31.4	22.8	14.0	8.8
Total	1231	346	356.0	162.9	181.8	127.3	54.5
Average	....	...	50.9	23.2	25.9	18.2	7.7

* Not included in average.

By absolute agreement, we mean that both tests checked, that is, 444, 443, 000, and so forth, an absolute, numerical quantitative agreement of both tests. To arrive at a relative agreement, we assume a Kahn reading of 244 or above to be positive and a Kolmer reading of 33, 34, 43 or 44 to be positive. Absolute disagreement indicates that a negative was present in one test while a positive reading was obtained in the other.

From the above tabulation, it will be seen that there is only 48.2 per cent absolute agreement and 20.4 per cent relative agreement in proved syphilitic cases. In known nonsyphilitic cases, the absolute agreement was 75.8 per cent, relative agreement, 22.8 per cent and combined agreement, 98.6 per cent. Hence the disagreement between the Kolmer modification of the Wassermann test and the Kahn tests is most striking in patients who have syphilis. The two tests apparently eliminate the nonsyphilitic cases equally well.

The greatest absolute agreement is seen in primary syphilis, secondary syphilis and cardiovascular syphilis and the least agreement in bone syphilis and central-nervous-system syphilis. The greatest combined agreement (absolute and relative) is seen in primary and secondary and cardiovascular syphilis while the least is noted in late cutaneous and central-nervous-system syphilis.

Bone syphilis was omitted because of the small number of cases studied and because there was no relative agreement. In central-nervous-system syphilis alone did relative agreement exceed absolute agreement.

The cases listed under investigations for syphilis which subsequently proved to be negative showed an absolute agreement of 73.1 per cent and a relative agreement of 25.3 per cent with a combined agreement of 98.6 per cent. Of the 1.6 per cent disagreement the Kolmer was negative in all tests.

The greatest total disagreement was in central-nervous-system syphilis (83 cases), 37.3 per cent and in late cutaneous syphilis (11 cases), 34 per cent. The least disagreement was noted in secondary syphilis 16.3 per cent and primary syphilis, 17 per cent.

In cardiovascular syphilis, it is to be noted that the Kahn test was the more sensitive test. Here the combined agreement was 82. 6 per cent in the Kolmer test and 91.8 per cent in the Kahn.

In neurosyphilis the disagreement was 37.3 per cent of which 10 per cent were Kahn positive and 27.3 per cent Kolmer positive.

Of the remaining types of syphilis, that is, primary and secondary syphilis, and latent syphilis, the disagreement between the Kolmer and Kahn results is less marked.

In the proved nonsyphilitic patients among whom there were 461 tests, 104 showed some slight degree of positivity in the Kahn test, that is, 001, 011, 012. Of the 104 patients, 78 were found with miscellaneous dermatoses and 26 among the negative investigations for syphilis. The Kolmer showed some degree of positivity in 5 tests among the dermatoses and in 4 tests of the proved nonsyphilitic investigations.

TABLE II.—NONSYPHILITIC CASES.

Type.	Tests.	Cases.	Absolute agreement.	Relative agreement.	No agreement.	Kolmer positive Kahn negative.	Kahn positive Kolmer negative.
Miscellaneous dermatoses	327	216	78.5	20.3	1.2	0.8	0.4
Syphilis investigations proved negative . .	134	64	73.1	25.3	1.6	...	1.6
Total	461	280	151.6	45.6	2.8	0.8	2.0
Average	...	...	75.8	22.8	1.4	0.4	1.0

Discussion. Our aim in presenting these results is to compare the Kolmer modification of the Wassermann test and the Kahn test with the clinical findings rather than the agreement between the two tests. To this end, we have divided our patients in two groups: proved syphilitic and proved nonsyphilitic cases. Of the 631 cases presented, 280 or 44.3 per cent were proved nonsyphilitic

and 351 or 55.7 per cent were proved syphilitic patients. On the proved nonsyphilitic patients, 461 tests (27 per cent of the total number of tests) were done. On the proved syphilitic patients 1241 tests (73 per cent of the total number of tests) were done. The dermatoses, proved to be nonsyphilitic, and the syphilitic investigations proved to be negative are grouped together in one tabulation while the proved syphilis is grouped in another.

Reactions of the type 001, 011, 012, were noted in the Kahn test in 104 of the 631 tests on proved nonsyphilitic patients. Of these, 78 were in patients with miscellaneous nonsyphilitic dermatoses and 26 in patients later proved nonsyphilitic. The same type of reaction was found in 5 tests on the proved nonsyphilitic dermatoses and 4 in later proved nonsyphilitic patients with the Kolmer method. If the Kahn persistently shows some degree of positivity and the Wassermann is negative and the case is clinically classified as nonsyphilitic, we may assume one of three things:

1. Syphilis may exist in the absence of clinical evidence other than the faintly positive serologic test. This contention could not be substantiated short of elaborate follow-up and autopsy study.

2. That the Kahn test in this type of case (nonsyphilitic) is oversensitive to some component of the patient's serum probably unrelated to the reagin in syphilitic blood serum which provokes the precipitation reaction in actual syphilis. Kahn, Landau and McDermot[13] have pointed out that this component in the patient's serum may likewise determine the complement-fixing power of the serum. This reaction of the Kahn test seems frankly nonspecific in character and, occurring as it did in 22.5 per cent of the proved nonsyphilitic cases, has a tendency to lessen its value in this connection.

3. The Kahn antigen may be subject to marked variations in behavior and may not lend itself well to individual production in laboratories utilizing this procedure. We feel that our method of rereading and checking the Kahn results largely minimizes the personal factor that might enter into a slightly positive precipitation reading.

Among the proved nonsyphilitic dermatoses, eczema showed 11.8 per cent disagreement, scabies 10.7 per cent, and urticaria 20 per cent. Both tests showed some degree of positivity in eczema—the Kahn test here giving three times as many positives as did the Kahn test in urticaria. In dermatomycosis and impetigo contagiosa the Kahn test alone gave some degree of positivity. In all the other types of dermatoses, 40 in all, 22 showed absolute agreement and 18 showed absolute and relative agreement but no disagreement.

We agree with Kahn[12] in his recent discussion and report that the simplicity of his test is over emphasized and that for the best results the antigen should be prepared as outlined by him and the tests performed by an experienced worker. In our laboratory, we

have adhered strictly to the method as outlined by Kahn and have devoted the necessary time for its accurate performance. The readings were made before and after being in the ice box overnight and by three different observers.

In the light of a recent survey of the literature, of the Kahn test by Stokes and Chambers,[14] our proportion of agreement between the two tests is low. We hope, however, that our results, classified into types of syphilis present and syphilis absent will have value in placing emphasis where it belongs, not on the results of paralleled tests alone but on the agreement of tests with clinical findings.

TABLE III.—DERMATOSES EXAMINED IN A COMPARATIVE STUDY OF KOLMER MODIFICATION OF THE WASSERMANN AND KAHN TESTS.

	Cases.	Tests.	Absolute agreement.	Relative agreement.	No agreement.	Kolmer positive Kahn negative.	Kahn positive Kolmer negative.
Acne vulgaris	23	32	71.9	28.1			
Alopecia	8	9	77.7	22.3			
Chancroid	1	3	66.6	23.4			
Dermatomycosis	28	37	62.2	35.1	2.7	..	*
Dermatitis venanata	4	4	50.0	50.0			
Stasis dermatitis	5	6	50.0	50.0			
Eczema	14	17	58.8	29.4	11.8	*	*
Fibroma	3	3	66.6	23.4			
Furunculosis	4	6	50.0	50.0			
Granuloma pyogenicum	2	10	50.0	20.0			
Herpes simplex and zoster	3	4	75.0	25.0			
Impetigo contagiosa	11	15	66.6	20.7	6.7	..	*
Keratosis pilaris	2	4	50.0	50.0			
Pediculosis	2	5	80.0	20.0			
Pruritus	6	6	83.3	16.7			
Pigmented nevus	3	3	33.3	66.7			
Pityriasis rosea	5	5	80.0	20.0			
Psoriasis	18	29	75.9	24.1			
Seborrhoeic dermatitis	7	8	87.5	12.5			
Scabies	16	28	78.6	10.7	10.7	*	‡
Tinea versicolor	2	2	50.0	50.0			
Urticaria	5	10	30.0	50.0	20.0	‡	*
Ulcus acutum vulvæ	2	4	25.0	75.0			

One hundred per cent agreement was found in Acne rosacea, Blastomycosis, Dermatitis repens, Traumatic dermatitis, Dermatitis exfoliativa, Occupational dermatitis, Epithelioma, Erythema multiforme, Erosio interdigitalis blastomycetes, Erythema nodosum, Folliculitis simplex, Keratosis senilis, Lichen planus, Majocchi's disease, Molluscum contagiosum, Pityriasis rubra pilaris, Pigmented dystrophy, Sycosis vulgaris, Tinea barbæ, Tinea circinata, Verrucæ and Vitiligo. Of these there were 36 cases with 39 tests.

* One case. ‡ Three cases.

Summary. 1. The Kolmer modification of the Wassermann test and the Kahn test were performed on identical sera in 631 cases with 1702 tests showing 75.8 per cent absolute agreement in proved

nonsyphilitic cases; 50.9 per cent absolute agreement in proved syphilitic cases.

2. Our relative agreement was found to be 22.8 per cent in proved nonsyphilitic patients and 23.2 per cent in proved syphilitic patients.

3. The absolute and relative agreement is 98.6 per cent in proved nonsyphilitic patients and 74.1 per cent in proved syphilitic patients. Our proportion of agreement is low as compared to results published by other observers.

4. We find that the Wassermann and Kahn tests eliminate syphilis in miscellaneous dermatoses equally well and that the disagreement is evidenced in proved cases of syphilis.

5. The least disagreement in proved syphilitic patients was in primary syphilis (17 per cent) and secondary syphilis (16.3 per cent).

6. The greatest disagreement was found to be in central-nervous-system syphilis (37.3 per cent) and late cutaneous syphilis (22.8 per cent).

7. In cardiovascular syphilis the Kahn test was the more sensitive of the two.

8. Conclusions on bone syphilis were discarded because of the few cases in that group.

9. We find an absolute agreement in 22 out of 40 types of miscellaneous nonsyphilitic dermatoses, with absolute and relative agreement in 18 and disagreement in 5.

10. We feel that an 001 or 012 Kahn result may be nonspecific.

11. Eczema, scabies and urticaria in nonsyphilitic patients showed disagreement between Kolmer and Kahn tests ranging from 10.7 per cent to 20 per cent.

12. More emphasis is placed in our discussion on the agreement of the tests with the clinical findings than on the agreement between the two tests. We believe that further investigations of this type are needed.

13. We believe both tests simultaneously performed on every serum are necessary to the syphilologist, and that he should insist upon a report including both.

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THE PHYSIOLOGY OF THE MILKING MUSCLE OF THE KIDNEY.

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(From the Department of Surgical Research and the Department of Urological Surgery, University of Pennsylvania. Aided by a grant from the Harriet M. Frazier Fund for Research in Surgery.)

In a study of the anatomy of the "Musculus Spiralis Papillæ,"[1] reconstruction models were made from serial sections of the human renal papilla with its calyx which showed the existence of two broad bands of smooth musculature in the calyceal wall surrounding the papilla like a spiral. It was shown to be present in every human kidney with identical topography in every instance. (Figs. 1 and 2.)

The constant presence of this spiral muscle in the kidney suggested the possibility that it was an anatomical necessity. A muscle of this type and location can do one thing only; while contracting it will squeeze the papilla and in that way empty its contents. This causes an act of suction on the papillary duct and thus milks the renal papilla. It seems then, that the urine does not drip out of each papilla due to the vis-a-tergo of the blood pressure, but that a physical agent, such as suction, has a great deal to do with the outflow of the urine from the kidney.

While looking over some pyelograms taken by Dr. H. Pancoast, we were fortunate in finding two pictures which showed most interesting facts. (Fig. 3.) The continuity of the pyelographic medium between the main pelvis and the calyces was definitely broken. In spite of complete distention of the pelvis, something cut the calyceal shadows off from the main pelvic shadow. Because of the location of the interruption, it seems probable that this might be

due to the action of the papillary muscle, which was caught in the act of contraction. The muscle contracted but was unable to empty the calyces completely because of the pressure under which the pyelographic fluid was held in the pelvis.

The physiology of the spiral muscle of the kidney was studied in the pig as the only animal, except the large ape, whose kidneys are similar to the human, having multiple single papillæ, surrounded by individual calyces. (Fig. 4.) The histology of the calyx in the pig is the same as in human, the bands of smooth musculature being present in a very pronounced manner, forming a ring or a spiral encircling the papilla.

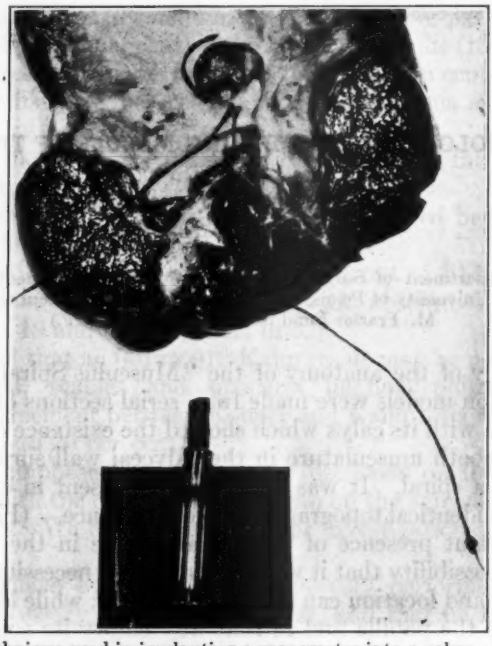

FIG. 5.—Technique used in implanting a manometer into a calyx. Upper picture shows a purse string being put around a calyceal mouth, the lower illustrates one of the mushroom like glass tubes which were implanted into the calyx.

The pigs' kidney were brought to the laboratory and the excised parts immersed in highly oxygenated Locke's solution within twenty-five minutes from the time the animal was killed. (Locke's solution: NaCl, 0.9 per cent, $CaCl_2$, 0.02 per cent, KCL, 0.042 per cent, with the addition of $NaHC0_3$, 0.03 per cent and glucose, 0.1 per cent just before the experiment began. Glass-redistilled water was used throughout.)

A papilla was excised with its surrounding calyx and some kidney

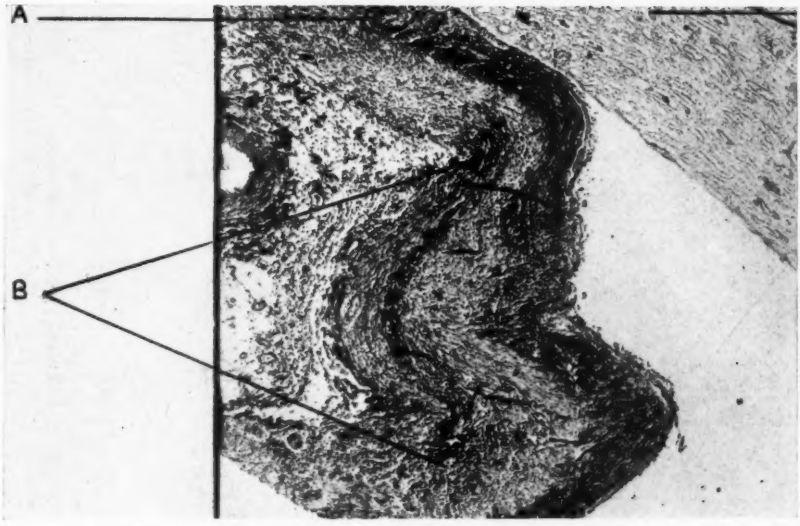

FIG. 1.—Microphotograph showing the calyx of the renal papilla. *A*. Upper part of the muscle at the base of the papilla, heavy bundles in cross section, extending into the subepithelial stratum of the calyx, the collagen of which appears black in the illustration. *B*. Lower part of the same muscle at the mouth of the calyx; numerous small and large bundles extend from the middle of the calyx down to the point of its junction with the main pelvis, which is at the bottom of the illustration. The muscle extends between the two lines marked *B* and is bordered by fainter stained loose connective tissue. (Mallory's connective tissue and muscle stain.) (Reproduced from *Journal of Urology*.)

FIG. 2.—Wax model of the musculus spiralis papillæ. Two broad rings of musculature are seen, one at the base, the other at the mouth of the calyx brought together by a middle piece, thus resembling a spiral. (Reproduced from *Journal of Urology*.)

FIG. 3.—Pyelogram of a human kidney. The calyceal shadows in the middle of the illustration are definitely cut off from the main pelvic shadow.

FIG. 4.—Pyelogram of a pig's kidney. The papillæ are single surrounded by individual calyces, closely resembling the human kidney.

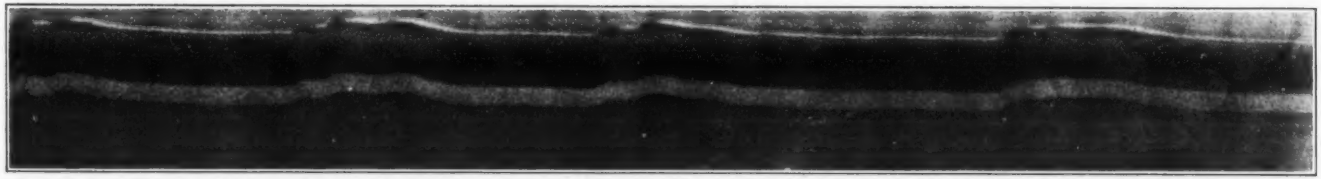

FIG. 7.—Photographic record of the contractions of the muscle. Contractions small, but regular, rhythmic and equal.

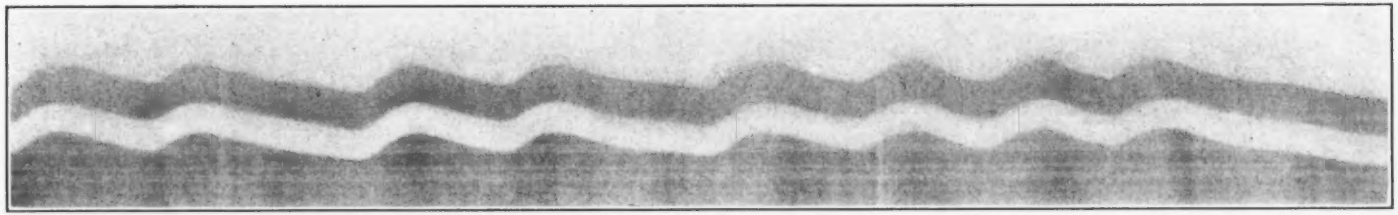

FIG. 8.—Photographic record of the contractions of the muscle. Contractions larger, regular and equal.

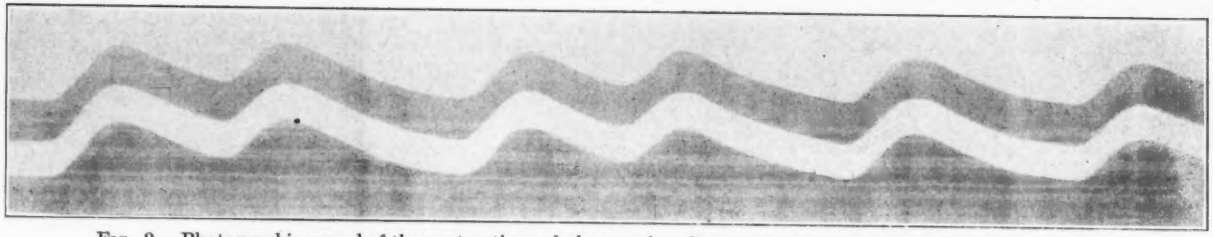

FIG. 9.—Photographic record of the contractions of the muscle. Contractions large, regular, rhythmic and equal.

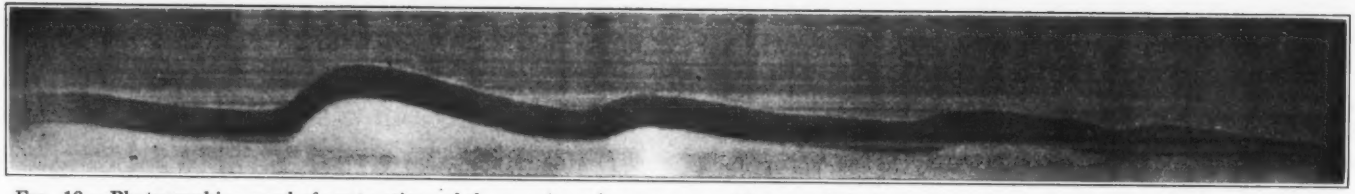

FIG. 10.—Photographic record of contractions of the muscle under pressure. After a period of rest, first a heavy contraction, followed by smaller ones and finally rest.

tissue. A purse-string of silk was then placed around the calyceal mouth, a glass tube with a wide mushroom-like lower opening was inserted into the calyx and the string tied. The excess renal tissue was then trimmed off until the red papillary tissue was seen. Having made sure that there was no leakage from the calyx, a capillary tube of 1 mm. bore was connected with the glass mushroom by a small piece of rubber tubing to make a tight joint. Any change of pressure inside of the calyx would, therefore, raise or lower the fluid in the capillary (Fig. 5).

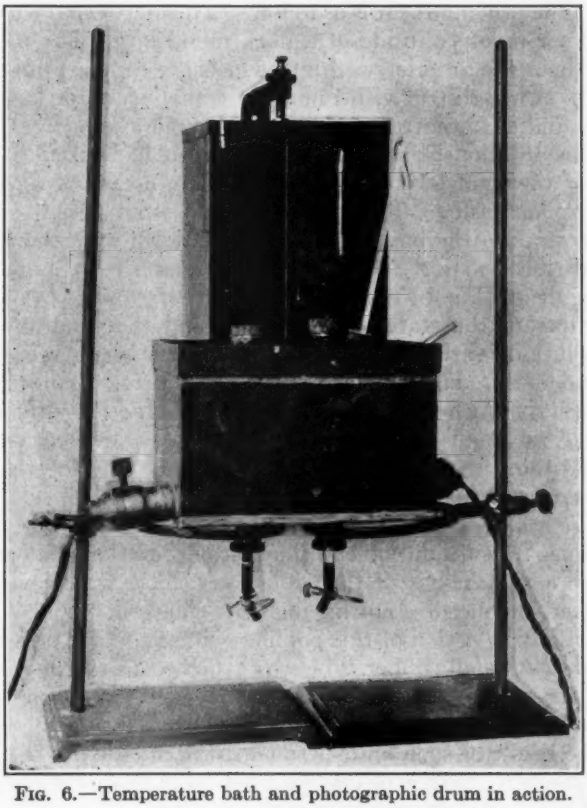

FIG. 6.—Temperature bath and photographic drum in action.

The preparation was then inserted into a constant temperature bath such as that used for the guinea-pig's uterus, with the highly oxygenated Locke's solution at a temperature of 38° C. After a short while fluctuations in the capillary manometer were noted.

These fluctuations representing the changes of intracalyceal pressure are regular and rhythmic, appearing about every thirty

seconds. The rise of fluid is usually gradual, but it often starts with a sudden jump to reach a certain height and then gradually returns to the former level, where it rests until the time of the next contraction.

The fluctuations, representing the contractions of the muscle, are uniform, equal, of the same vigor and the same height for each preparation, as can readily be seen from the illustrations. (Figs. 7, 8 and 9.)

These photographic records were made by a specially developed technique, the details of which are being published in another paper.[2] The principle of it is as follows: a drum covered with brom-silver paper revolves inside of a dark metal box. The box has a 1 mm. slit in the anterior wall into which the capillary manometer is placed. A metal strip with 1 mm. slit is then placed in front of the capillary and a concentrated light thrown upon the box. A drop of the yellow solution of azo-benzene dissolved in benzene is placed on top of the fluid level in the capillary by means of a very fine needle capillary tube. The yellow drop does not permit any light to penetrate into the box, moving up and down with the capillary fluid and thus charting a white curve on the sensitized paper of the revolving drum (Fig. 6).

According to the state of the muscle and the condition of the saline solution, various degrees of contractile vigor were noted; slight, moderate, and strong, the lowest rise being 1 cm. in height, the highest as much as 10 cm. Once the contractions started they continued for about twenty to thirty minutes and even as long as an hour without changing in height or rhythm, save for a period of rest after every 6 to 8 contractions.

Figs. 7, 8 and 9 show the actual photographic records of these fluctuations, the height of the fluctuations in these photographs being the actual height of the excursions of the fluid level of the manometer, the pictures not having been enlarged.

A study of the action of this papillary muscle under pressure was also made. A small rubber tube was attached to the upper end of the capillary manometer, the fluid level lowered for 1 inch by blowing in some air and clamping the tube with a hemostat. Fig. 10 shows the result of such an experiment; the muscle acted, working against pressure, first a heavy contraction, followed by a smaller one, and then complete rest.

These experiments show definitely that the papillary muscle of the kidney is an anatomic and physiologic entity. Calculations have shown that the amount of fluid which rose in the manometer tube at each contraction is about equal to the volume of the given calyx. Thus, when the papillary muscle contracts it expresses the entire fluid of the calyx, transmitting this pressure wave upon the papilla and squeezing it for a short interval, releasing it only after the

muscle has relaxed and rests. The spiral architecture of this muscle indicates that the impulse begins at the base of the papilla, travelling around it until it reaches the calyceal mouth. This action can only be compared with the act of milking, causing suction upon the papilla. This milking effect must cause a period of negative pressure in the calyx and also in the main ductus urinarius, the central duct of the papilla, sucking the urine out of the kidney substance.

The vital rhythm of the papillary muscle, contracting every thirty seconds, is analogous to the rhythm of the urinary flow from the papilla. Dr. Carl Schmidt and I were able to demonstrate this by exposing a single papilla of the pig's kidney under ether anesthesia and implanting a mushroom glass tube with a purse-string into the calyx. Studying the rate of the urinary flow from this isolated papilla in the following days, the pig being conscious, we established the fact that the urine does not appear in a continuous flow but in drops, a drop of urine approximately every thirty seconds. It would seem, therefore, that the rhythm of the papillary muscle and the rhythm of the urinary flow from the renal papilla are the same; every thirty seconds there occurs a contraction of the papillary muscle of the kidney, producing a drop of urine.

Consideration of the pathology of this milking muscle and its relation to various unexplained kidney diseases is a fascinating subject. The repeatedly proved and yet seriously doubted reno-renal reflex and the vesico-renal reflex may herein find anatomic expression and foundation. What relation will it hold to clinical conditions under hypertonic and hypotonic action? Could we not explain postoperative reflex anuria by paralysis of this muscle and certain variations of the urinary secretion of the kidney by partial hypo- or hyperfunction of it?

Summary. Data are presented which demonstrate rhythmic contraction of the spiral muscle of the renal papilla. It seems highly probable that this muscle causes an act of suction on the papillary duct and this milks the renal papilla. The force of the contraction varies for each preparation, but the time relation for contraction remains the same, about every thirty seconds.

I wish to express my sincere gratitude to Dr. Alexander Randall, Dr. A. N. Richards and Dr. I. S. Ravdin for their interest in this work and help they have given.

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STATISTICAL REPORT ON THE TREATMENT OF HAY FEVER.

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It is not my purpose at this time to discuss the comparative merits of the various pollen extracts—particularly as I believe that, having established the satisfactory activity of a freshly prepared pollen extract, the beneficial result is dependent chiefly on the total maximum dose one is able to reach before the expected date of pollination.

Many methods and plans for the pre-seasonal and seasonal treatment of hay fever are constantly being advocated, each in turn being recommended on the basis of its greater efficacy. In the present series of 425 cases[1] the writer has systematically employed, singly and in combination, these various methods of treatment. The purpose of this article therefore is to present, in as concise a manner as possible, the results of a careful study of these various types of therapy.

Hay fever, more fittingly called pollen rhinitis, can usually be diagnosed accurately by means of a skin test, employing either the scratch or the intradermal method. While both have their advantages and disadvantages, I believe the accuracy of results depends, not so much on the type of technique, as on the experience of the operator with the particular method employed.

In studying large numbers of cases of pollen rhinitis one encounters quite a few with a clear-cut history, but which give no positive skin reaction to pollens. These cases generally react by applying concentrated pollen to the nasal mucosa, and may be protected by pollen treatment. We have, however, had several of these cases with a history of symptoms starting at a definite time of the year (August), and running a similar course annually, that did not react to any of the pollens used in testing, could not produce symptoms by nasal test, and were not protected by pollen (ragweed) treatment. The cause of symptoms in these patients is still problematical.

Three distinct types of cases are included in this study: Type A: *Ragweed Cases*, these cases reacted to one pollen (ragweed) and were *treated with ragweed* alone. Type B: *Grass Cases*, all reacting to timothy, and some to June grass, orchard grass or red top. These cases reacted to several pollens and were *treated with timothy*, the one which gave the largest reaction. Type C: *Grass Cases* reacting to timothy and several grasses. These were *treated with all pollens which gave a strong reaction.*

[1] This series was selected from cases treated in private practice and at the Departments of Applied Immunology of the French Hospital and Fifth Avenue Hospital, New York City, from 1919 to 1927.

For the purpose of clarity, and to avoid repetition, these types will be designated throughout this entire report as TYPE A, TYPE B and TYPE C respectively.

The cases are further classified into three series. Pre-seasonal treatment was given in all the 425 cases, the classification into series being solely on the bases of differences in the manner of carrying out pre-seasonal treatment.

Series I includes all cases receiving pre-seasonal treatment for three months before the date of pollination. Injections were given twice a week up to the date of pollination. There were 220 cases in this series.

Series II includes all cases receiving intensive pre-seasonal treatment in which the dose was rapidly increased. Treatment was started three months before the expected onset of symptoms. Injections were given every day for two weeks; then dropped to twice a week, until the date of expected onset. This series consisted of 120 cases.

Series III includes all cases which were given two weeks' intensive pre-seasonal treatment, starting two weeks before the date of onset of symptoms, injections twice a day, the dose of pollen being increased at each dose up to the expected date of pollination. There were 85 cases in Series III. Each series was further subdivided into *classes*, and these in turn, into *groups*, as will be seen in the tables.

Series I: (THREE MONTHS PRE-SEASONAL TREATMENT: INJECTIONS TWICE A WEEK UP TO DATE OF POLLINATION.) Table I gives the results in *Class* 1, cases receiving only pre-seasonal, no seasonal treatment. This class included 30 cases: 10 cases of TYPE A, (Ragweed cases treated with ragweed), 10 cases of TYPE B (Grass cases treated with timothy), and 10 cases of TYPE C (Grass cases treated with several grass pollens to which the patients reacted).

TABLE I.

Type	No. of cases.	Results.
A	1	Complete relief
	1	50 per cent improvement
	5	25 per cent improvement
	3	No improvement
B	4	50 per cent improvement
	3	25 per cent improvement
	3	No improvement
C	4	95 per cent improvement
	4	50 per cent improvement
	2	No improvement

Table II gives the results in *Class* 2, 60 cases receiving both pre-seasonal and seasonal treatment. Seasonal injections were given to half the cases once a week and the other half twice a week, using one-half the maximum dose reached before the date of pollination.

The cases in each type were divided equally as to number, into two groups. The one point in which therapy differed in these two groups was in the frequency of seasonal injections: In *Group* 1 they were given once a week; in *Group* 2, twice a week.

TABLE II.

Type.	Group.	No. of cases.	Results.
A	1	3	Complete relief
		4	60 per cent improvement
		1	25 per cent improvement
		2	No improvement
	2	6	Complete relief
		3	80 per cent relief
		1	No relief
B	1	3	Complete relief
		3	50 per cent relief
		2	25 per cent relief
		2	No improvement
	2	5	Complete relief
		2	75 per cent improvement
		2	50 per cent improvement
		1	No improvement
C	1	6	Complete relief
		3	80 per cent relief
		1	50 per cent relief
	2	7	Complete relief
		2	80 per cent relief
		1	50 per cent relief

Table III gives the results in *Class* 3, 15 cases receiving pre-seasonal treatment, as in all of Series I, also local treatment of the nose, but no seasonal pollen injections.

TABLE III.

Type.	No. of cases.	Results.
A	1	Complete relief
	3	50 per cent relief
	1	No relief
B	1	50 per cent relief
	2	25 per cent relief
	2	10 per cent relief
C	1	Complete relief
	2	50 per cent relief
	1	25 per cent relief
	1	No relief

In Table IV are shown the results in *Class* 4, 15 cases receiving pre-seasonal treatment, as in all of Series I, also seasonal treatment including nasal desensitization and pollen injections both continued throughout the season.

TABLE IV.

Type.	No. of cases.	Results.
A	3	Complete relief
	1	75 per cent relief
	1	25 per cent relief
B	1	Complete relief
	2	25 per cent relief
	2	50 per cent relief
C	3	Complete relief
	1	80 per cent relief
	1	60 per cent relief

Table V gives the results in *Class* 5, 15 cases receiving pre-seasonal treatment, as in all of Series I, and also treated with the Kromeyer lamp, but no seasonal pollen injections. The Kromeyer lamp treatment was given with a hollow tube applicator, beginning with one-half minute in each side of the nose and increasing up to five minutes in each side.

TABLE V.

Type.	No. of cases.	Results.
A	1	35 per cent relief
	1	25 per cent relief
	1	10 per cent relief
	2	No relief
B	1	35 per cent relief
	2	25 per cent relief
	2	No relief
C	2	50 per cent relief
	1	25 per cent relief
	2	5 per cent relief

In Table VI are given the results in *Class* 6, comprising 15 cases which received pre-seasonal treatment, as in all of Series I, with in addition both pre-seasonal and seasonal treatment with the Kromeyer lamp and seasonal pollen treatment.

TABLE VI.

Type.	No. of cases.	Results.
A	2	95 per cent relief
	2	50 per cent relief
	1	10 per cent relief
B	1	95 per cent relief
	2	50 per cent relief
	1	30 per cent relief
	1	No relief
C	3	95 per cent relief
	1	50 per cent relief
	1	25 per cent relief

In Table VII are shown the results in *Class* 7, 15 cases receiving pre-seasonal treatment, as in all of Series I, also pre-seasonal Kro-

meyer lamp treatment and seasonal local and injection treatment, and Kromeyer lamp.

TABLE VII.

Type.	No. of cases.	Results.
A	3	95 per cent relief
	1	80 per cent relief
	1	75 per cent relief
B	2	80 per cent relief
	1	50 per cent relief
	1	25 per cent relief
C	3	80 per cent relief
	2	50 per cent relief

In Table VIII are given the results in *Class* 8, compressing 55 cases, all of them Type A (ragweed). All received pre-seasonal treatment, as in all of Series I, and an autogenous nasal vaccine. In addition, seasonal treatment, injection of pollen and vaccine, local nasal pollen applications, and Kromeyer lamp treatment were variously administered as indicated in the table.

TABLE VIII.

Type of treatment.	No. of cases.	Results.
Group 1.		
Pre-seasonal pollen and autogenous nasal vaccine	1	50 per cent relief
	1	25 per cent relief
	1	10 per cent relief
	2	No relief
Group 2.		
Same as Group 1; also seasonal pollen and vaccine injections	3	95 per cent relief
	1	90 per cent relief
	1	50 per cent relief
Group 3.		
Same as Group 1; also local nasal pollen applications	1	80 per cent relief
	1	50 per cent relief
	2	25 per cent relief
	1	10 per cent relief
Group 4.		
Pre-seasonal and seasonal pollen and vaccine injections and local nasal pollen applications	6	90 per cent relief
	3	75 per cent relief
	1	25 per cent relief
Group 5.		
Pre-seasonal as in Group 4; also Kromeyer lamp to nasal mucosa. No seasonal treatment	3	50 per cent relief
	2	40 per cent relief
	3	25 per cent relief
	1	10 per cent relief
	1	No relief
Group 6.		
Pre-seasonal as in Group 5, and this continued throughout season	6	90 per cent relief
	4	75 per cent relief
Group 7.		
Same as Group 6, without local nasal pollen	5	90 per cent relief
	3	75 per cent relief
	2	25 per cent relief

Series II (THREE MONTHS INTENSIVE PRE-SEASONAL TREATMENT: RAPID INCREASE OF DOSE. TREATMENT EVERY DAY FOR TWO WEEKS; THEN TWICE A WEEK UNTIL EXPECTED DATE OF ONSET). Table IX gives the results in *Class* 1, cases receiving preseasonal treatment, as in all of Series II, and no seasonal treatment This class included 25 cases: 10 cases of TYPE A (ragweed cases treated with ragweed), 5 cases of TYPE B (grass cases treated with timothy), and 10 cases of TYPE C (grass cases treated with several grass pollens to which the patients reacted).

TABLE IX.

Type.	No. of cases.	Results.
A	4	75 per cent relief
	4	50 per cent relief
	1	25 per cent relief
	1	No relief
B	1	75 per cent relief
	1	50 per cent relief
	2	25 per cent relief
	1	No relief
C	3	75 per cent relief
	3	50 per cent relief
	3	25 per cent relief
	1	No relief

Table X gives the results in *Class* 2, 50 cases receiving both preseasonal treatment, as in all of Series II, and also seasonal treatment, once or twice a week using one-half the maximum dose reached before the date of pollination.

The cases in each type were divided equally as to number, into two groups. The one point in which therapy differed in these two groups was in the frequency of seasonal injections: In *Group* 1 they were given once a week: in *Group* 2, twice a week.

TABLE X.

Type.		No. of cases.	Results.
A	1	5	95 per cent relief
		4	75 per cent relief
		1	50 per cent relief
	2	5	95 per cent relief
		5	75 per cent relief
B	1	2	85 per cent relief
		2	50 per cent relief
		1	35 per cent relief
	2	3	85 per cent relief
		2	50 per cent relief
C	1	6	90 per cent relief
		3	80 per cent relief
		1	60 per cent relief
	2	6	95 per cent relief
		4	85 per cent relief

In Table XI are found the results in *Class* 3, compressing 15 cases that received pre-seasonal treatment, as in all of Series II, and also local treatment of the nose, but no seasonal treatment.

TABLE XI.

Type of treatment.	No. of cases.	Results.
A	2	50 per cent relief
	2	25 per cent relief
	1	10 per cent relief
B	2	50 per cent relief
	2	25 per cent relief
	1	10 per cent relief
C	2	50 per cent relief
	2	25 per cent relief
	1	10 per cent relief

In Table XII are given the results in *Class* 4, including 30 cases which were given pre-seasonal treatment, as in all of Series II, and also nasal desensitization, both continued throughout the season.

TABLE XII.

Type.	No. of cases.	Results.
A	2	100 per cent relief
	6	95 per cent relief
	2	75 per cent relief
B	6	90 per cent relief
	3	75 per cent relief
	1	25 per cent relief
C	6	100 per cent relief
	3	90 per cent relief
	1	85 per cent relief

Series III (Two Weeks Intensive Pre-seasonal Method: Treatment Twice a Day. Dose of Pollen Increased at Each Dose up to Expected Date of Pollination.) Table XIII gives the results in *Class* 1, which included 15 cases that received no seasonal treatment.

TABLE XIII.

Type.	No. of cases.	Results.
A	1	50 per cent relief
	2	10 per cent relief
	2	5 per cent relief
B	1	50 per cent relief
	1	10 per cent relief
	3	5 per cent relief
C	2	50 per cent relief
	2	10 per cent relief
	1	No relief

Table XIV gives the results in *Class* 2, including 20 ragweed (Type A) cases, and treated as noted in the table:

TABLE XIV.

Type of treatment.	No. of cases.	Results.
Group 1.		
In addition to the pre-seasonal treatment, seasonal injections were given twice a week, using one-half maximum dose reached before date of pollination	2	90 per cent relief
	2	50 per cent relief
	1	10 per cent relief
Group 2.		
In addition to the pre-seasonal treatment, local nasal pollen treatment was given. No seasonal treatment	2	50 per cent relief
	2	10 per cent relief
	1	No relief
Group 3.		
In addition to the pre-seasonal treatment, local nasal pollen treatment was given. Both continued throughout season . . .	2	80 per cent relief
	2	70 per cent relief
	1	25 per cent relief
Group 4.		
In addition to the pre-seasonal treatment, local nasal pollen treatment and seasonal injections were given, but no seasonal local nasal pollen applications	2	80 per cent relief
	2	50 per cent relief
	1	25 per cent relief

Table XV gives the results in *Class* 3, comprising 25 ragweed (TYPE A) cases, which received pre-seasonal treatment, as in all of Series III, also were given treatment with the Kromeyer lamp, and additional treatment as indicated for each Group in the table.

TABLE XV.

Type of treatment.	No. of cases.	Results.
Group 1.		
Kromeyer lamp once a day . No seasonal treatment	2	10 per cent relief
	3	No relief
Group 2.		
Kromeyer lamp twice a day. No seasonal treatment	2	10 per cent relief
	3	No relief
Group 3.		
Kromeyer lamp once a day, pre-seasonal and during season. No pollen injections during season	3	10 per cent relief
	2	No relief
Group 4.		
Series III pre-seasonal type of treatment, with additiona local pollen applications to nose. No seasonal treatment	1	10 per cent relief
	4	No relief
Group 5.		
Same as Group 4, and continued throughout season	1	75 per cent relief
	3	50 per cent relief
	1	25 per cent relief

Table XVI gives the results in *Class* 4, including 25 ragweed (TYPE A) cases, which were given pre-seasonal treatment, as in all of Series III, also treatment with autogenous vaccine. Other variations of treatment are noted for each group in the table.

TABLE XVI.

Type of treatment.	No. of cases.	Results.
Group 1.		
Pre-seasonal (see above). No seasonal treatment	1	10 per cent relief
	4	No relief
Group 2.		
Pre-seasonal (see above). Seasonal—only vaccine. No pollen injections	1	10 per cent relief
	4	No relief
Group 3.		
Pre-seasonal as in Group 2; in addition, Kromeyer lamp and local nasal pollen. No seasonal treatment	2	50 per cent relief
	2	25 per cent relief
	1	10 per cent relief
Group 4.		
Pre-seasonal same as Group 3; seasonal, all pre-seasonal methods continued throughout season	2	75 per cent relief
	2	50 per cent relief
	1	25 per cent relief
Group 5.		
Same as Group 4, except for omission of nasal pollen applications during season	2	70 per cent relief
	2	50 per cent relief
	1	10 per cent relief

Conclusions. On the basis of this study of 425 cases, the writer is of the opinion that:

1. It is important to give a large amount of pollen before the onset of the pollen season.

2. It is quite evident that it is absolutely essential to continue treatment throughout the entire season.

3. Local desensitization increases relief.

4. Autogenous vaccines (from nose), given together with pollen, before and during the season, is helpful.

5. Local treatment of the nose with the Kromeyer lamp helps some patients and has no effect on others. It seems to lower local irritability of the nasal mucosa. In fact, generally speaking, it is more helpful in nonspecific vasomotor rhinitis than in specific pollen cases.

6. Autogenous vaccines (nose) alone, without the use of pollen in specific cases, are of no value.

7. Local pollen treatments alone, without pollen injections, give no relief whatsoever.

8. While results obtained when using several pollens are apparently better than when a single pollen is used, the more advantageous results, are due not to the number of pollens employed but to the fact that a much larger dose of total pollen protein was injected than in cases injected with a single pollen.

9. It is evident that the best results are obtained in cases coming about three months before expected date of pollination, receiving two weeks' intensive treatment, increasing the dose of pollen rapidly and continuing injections up to the pollen season, reaching as high a dose as possible, then continuing injections of pollen twice a week

throughout the entire season; in addition, injections of autogenous vaccine prepared from the nose, and local treatment to the nose and eyes with increasing concentrations of pollen solutions, pre-seasonal and seasonal.

10. It has been found that mild symptoms in patients fairly well immunized can be controlled by the use of ephedrin, particularly if combined with a small dose of codein and atropin. In untreated cases, ephedrin is uncertain in its action: some cases are helped and others not at all.

The writer wishes to acknowledge the valuable services of Miss M. D. Hirsch, in the compilation of data presented in this report.

OBSERVATIONS ON THE EFFECTS OF SUBSTANCES OTHER THAN CARBOHYDRATE IN RELIEVING THE TOXIC SYMPTOMS OF INSULIN.

(Preliminary Report.)

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The rapidity with which most patients who have the symptoms of toxic effects of insulin recover after the oral administration of glucose or some other carbohydrate has impressed everyone who has observed it. It would appear to be a simple matter to explain this rapidity of recovery after subcutaneous injections of epinephrin or glucose. Since oral administration of carbohydrate[1] likewise results in prompt relief of symptoms of insulin overdosage, the possibility that the effect is due to some other mechanism than absorption suggests itself.

To test this, substances other than glucose or carbohydrate-containing foods were tried on patients in the hospital having diabetes, who showed the characteristic symptoms of insulin overdosage. These substances consisted of pure protein in 1 case, and mineral oil in 5 other cases.

Case Reports. Case I.—(R. S.) The patient had symptoms of insulin overdosage at 3.30 P.M. on January 18, 1928. Her course was as follows:

3.30 P.M. Blood sugar was 0.049 per cent. Patient complained of severe hunger, she felt very faint: there was profuse diaphoresis: pulse rate, 110 per minute: patient was given the whites of two eggs.

3.35 P.M. Skin was dry; pulse rate was 90 per minute; the patient felt perfectly comfortable.

3.45 P.M. Blood sugar was 0.057 per cent.
3.47 P.M. Patient was given 100 cc. of orange juice and one teaspoonful of sugar.
4.10 P.M. Blood sugar was 0.066 per cent.

Comment. The striking fact here is the prompt subjective recovery after oral administration of protein. This being the first experiment tried, orange juice and sugar were given subsequently in order to be safe. (However, one is impressed by the fact that the increase in blood sugar is no more after 17 gm. of carbohydrate than it was after 12 gm. of protein.)

CASE II.—(J. S.) The patient had symptoms of insulin overdosage at 4.30 P.M. on March 8, 1928. His course was as follows:
4.30 P.M. Blood sugar was 0.061 per cent. Patient had profuse diaphoresis, was very faint and was somewhat disoriented as to time and place. He was given 2 ounces of mineral oil.
4.35 P.M. The sweating had stopped but the patient still felt faint.
4.50 P.M. The patient had completely recovered in spite of the fact that the blood sugar was 0.060 per cent.
5.15 P.M. The patient's condition was normal. Blood sugar was 0.057 per cent.

Comment. The recovery here was prompt and striking, in spite of the fact that the blood-sugar level had not increased even forty-five minutes after the onset of symptoms. The patient was given no carbohydrate antidote and continued well.

CASE III.—(H.) The patient had symptoms of insulin overdosage at 6.30 P.M. on April 3, 1928. His course was as follows:
6.30 P.M. Blood sugar was 0.027 per cent. (This does not represent the true value since the blood specimen was not examined until twelve hours after it had been taken and some allowance must be made for glycolysis.) He had profuse sweating and the nurse found him out of bed staggering around his room. He was entirely disoriented. He was given 3 ounces of mineral oil.
6.40 P.M. Skin was dry, staggering had stopped: he went back to bed and had no more evidences of insulin overdosage.

Comment. We regret that a second blood-sugar determination was not obtained but one fact stands out, namely, that the symptoms were relieved apparently by the oral administration of mineral oil.

CASE IV.—(C. K.) The symptoms of insulin overdosage were induced by giving the patient an extra 40 units of insulin. The course was as follows:
2.30 P.M. Blood sugar was 0.039 per cent. Patient was perspiring slightly. There were no other complaints.
3.00 P.M. Blood sugar was 0.034 per cent. The sweating had increased: pulse rate had dropped to 60 per minute. Patient was given 2 ounces of mineral oil.
3.05 P.M. Blood sugar was 0.032 per cent.
3.20 P.M. Blood sugar was 0.032 per cent. No improvement in condition of patient.
3.55 P.M. Blood sugar was 0.029 per cent. Three more ounces of mineral oil were given.
4.10 P.M. Blood sugar was 0.028 per cent, pulse was arrhythmical and rate was 42 per minute. Patient was very drowsy, skin was very moist,

cold and clammy. One hundred cubic centimeters of orange juice plus two teaspoons of sugar were given.

4.15 P.M. Patient recovered entirely.

4.30 P.M. Blood sugar was 0.042 per cent.

Comment. Obviously, this attempt to antidote the symptoms of overdosage with mineral oil was a failure.

CASE V.—(H. G.) Symptoms of insulin overdosage were induced by 20 additional units. The results were as follows:

1.30 P.M. The patient complained of vertigo and weakness.

2.00 P.M. Blood sugar was 0.057 per cent. The weakness became more pronounced and he was perspiring profusely. The pulse rate was 110 per minute. He was given 3 ounces of mineral oil by mouth.

2.05 P.M. The patient recovered completely. The pulse rate was 80 per minute. He had no complaints.

2.15 P.M. Blood sugar was 0.059 per cent.

2.45 P.M. Blood sugar was 0.069 per cent.

Comment. It is of interest to note that ten minutes after the patient had entirely recovered from his symptoms, his blood sugar was practically the same as when he was in the midst of them.

CASE VI.—P. T. The patient had symptoms of insulin overdosage at 7 P.M. on July 25, 1928. His course was as follows:

7 P.M.: Blood sugar was 0.043 per cent. The patient was sweating. He became so maniacal that it was necessary to forcibly restrain him. He was given 2 ounces of mineral oil.

7.15 P.M.: The skin was dry and he was perfectly quiet.

July 31: He again showed the above symptoms.

7.30 P.M.: Blood sugar was 0.040 per cent. He was given 2 ounces of mineral oil.

7.40 P.M.: Subjectively the patient was normal.

8.30 P.M.: Blood sugar was 0.042 per cent. The patient was still normal.

9.30 P.M.: The patient became violent again. He was given 2 ounces of mineral oil and recovered completely. However, one hour later he was given 100 cc. of orange juice in order to obviate any difficulty during the night.

Comment. In this patient, mineral oil produced prompt recovery each time, although after the second time the recovery was not permanent and another dose of mineral oil was necessary. Since orange juice was given one hour later, it is difficult to say whether he would have gone through the night without further difficulty or not. In this case there was no change in the blood-sugar level.

Conclusions. Five of 6 cases of diabetes mellitus with symptoms of insulin overdosage showed complete and prompt symptomatic recovery, following the oral administration of substances other than carbohydrate.

Four recovered following the administration of mineral oil and one following the administration of pure protein. No explanation of these results is offered but further work is contemplated in the hope of discovering the mechanism involved.

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1. Foshay, L.: Insulin Reactions, Arch. Int. Med., 1927, **40**, 661.

REVIEWS.

FRACTURES AND DISLOCATIONS. By KELLOGG SPEED, S.B., M.D., F.A.C.S. Second edition. Pp. 952; 987 illustrations. Philadelphia: Lea & Febiger, 1928. Price, $11.00.

IN this second edition, as in the first, the entire subject of fractures and dislocations is covered. In this edition the author has omitted the preliminary chapters on pathology, symptoms, signs and diagnosis, the points covered by these being taken up in connection with each bone discussed. All references to the literature have been omitted. No fads have been included. Treatments both closed and open have been amplified to meet the requirements of present day usage. Only basic improvements in fracture care have been added.

The work shows the beneficial results obtained when the authority on the subject writes the text and selects the illustrations himself. In this instance, his experience in the war past as well as in civil practice in one of the large hospitals of this country, makes him doubly capable.

The work is an excellent one, and one the reviewer takes the greatest pleasure in recommending to the profession.

E. E.

SURGICAL DIAGNOSIS IN TABULAR OUTLINE. By DR. A. J. CEMACH, Vienna, Austria. Translated by EDWARD L. BORTZ, M.D. Fourth edition. With 109 tabular forms and 129 plates, with 584 subjects, many in colors. Philadelphia: F. A. Davis Company, 1928. Price, $12.00.

WHEN a technical work reaches its fourth edition, its value is sufficiently attested. It is now translated into the English language and should enjoy even a more widespread popularity.

The character of the work is distinctly a technical desk reference one. It is not a textbook, but for daily quick reference it is much better than such. The book is nicely gotten up, well printed, on good paper, carefully edited and most carefully and thoroughly illustrated.

It makes very interesting and instructive reading both for the undergraduate as well as the experienced graduate.

E. E.

HARVEY TERCENTENARY BOOKS.

(1) EXERCITATIO ANATOMICA DE MOTU CORDIS, 1628. Pp. 72; 4 illustrations. Facsimile edition by R. Lier & Co., Florence, 1928. Price: Half linen, $4.00; half leather, $5.00.

(2) EXERCITATIO ANATOMICA DE MOTU CORDIS ET SANGUINIS IN ANIMALIBUS. With an English translation and Annotations by CHAUNCEY D. LEAKE. Pp. 154; 10 illustrations. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1928. Price, $3.50.

(3) THE ANATOMICAL EXERCISES OF WILLIAM HARVEY. DE MOTU CORDIS, 1628: DE CIRCULATIONE SANGUINIS, 1649. The first English text of 1653 newly edited by GEOFFREY KEYNES. Pp. 202; 4 illustrations. London: Nonesuch Press, 1928. Price, $10.00.

(4) A BIBLIOGRAPHY OF THE WRITINGS OF WILLIAM HARVEY. By GEOFFREY KEYNES. Pp. 67; 20 illustrations. Cambridge: University Press, 1928. Price, 21 s.

THE singular good fortune which Harvey met throughout his career follows him felicitously in 1928, the year of the tercentenary of the publication of his great book. There has been a flood of special articles and of oratory to keep his memory green. The numerous Harvey dinners from London and New York to Colorado Springs served, on the Eastern continent with, but in the Western unfortunately without, the precious juice that mellows speech and the imagination to bear witness to the wisdom of Harvey's recommendation to his own college, on how such anniversaries should be celebrated. All testify to the esteem which this great contributor to physiology still enjoys. But he is even more fortunate in that his very works are again issuing from the press to commemorate his achievement. There are two facsimile translations, one from Italy (1) and one from the United States (2); two translations, one a reprint of the first English version of 1653, edited by Geoffrey Keynes, in a beautiful edition (3), and another a new rendering in modern prose by Chauncey D. Leake, of the University of California (2). To cap all, comes Keynes' valuable and interesting bibliography of the editions of Harvey (4). Here surely is fitting tribute to the memory of a great man.

Keynes' bibliography of Harvey's writings is a handsome quarto volume of sixty-seven pages. To each of the five sections, de Motu Cordis, de Circulatione sanguinis, de Generatione animalium, Opera omnia and Miscellanea, a bibliographic preface is prefixed. These prefaces contain matters of interest to collectors of Harveiana. The book is embellished, furthermore, with illustrations, very well reproduced, of title pages of twelve editions of Harvey's various

writings as well as three illustrations of the venous valves, one from an engraving in de Venarum ostiolis of Fabricius, 1624, which seems to have served as the model for Harvey's plate in the first edition of 1628. Keynes has added to the bibliography which Mr. Charles Perry Fisher published in the *Transactions* of the College of Physicians of Philadelphia in 1912 several new items. Despite his care, this bibliography has already an omission—the new translation of Chauncey D. Leake, presently to be described.

It is scarcely necessary to refer to Harvey's investigations. Those on the circulation have been amply described in connection with his tercentenary. Pity it is, however, that the much more lively study contained in his de Generatione is so little known and so little read. It is a fund of ingenious observation and of interesting speculation not on embryology only but on many subjects, including the methods of research in natural history. The new Harvey books which have been mentioned challenge discussion on their own account. All deserve praise. If the reprint of 1653 by the Nonesuch Press is the most handsome—really an altogether delightful volume in form, in the color of its red leather dress, in its paper and print, the volume published by Mr. Thomas encourages one to hope that this is only the first of a series of translations of scientific treatises to which he will accustom us; it is adequate, printed with good type on good paper, with illustrations in half tone which, if not always perfect, yet form a possession for which to be grateful. And its price is after all about a third only of the Nonesuch edition. It is perhaps a pity that the two letters to Riolanus were omitted from this new translation; they add fullness at least to certain of Harvey's views. Had he dealt with them, Professor Leake might not have made that reference to Galilei which is found in a footnote on page 70.

Three English translations are now in our possession—the first anonymous one which appeared in 1653, four years before Harvey died and reprinted in 1673, the second one by Robert Willis done in 1847 for the Sydenham Society and the basis of several reprints and now the third by Professor Leake. Fortunately they differ strikingly. Each could scarcely escape the English of its time or of coloring Harvey's thought by the medium, the temper of the language which it uses. Keynes and Leake are agreed that Willis will not do. But in this alone they agree. Each has found a different way out: Keynes, a student of history and a lover of English, has returned to the post-Elizabethans; Leake, a modern and a teacher of moderns, has remained, as he believes Mr. Mencken would commend him for doing, loyal to his own time. If the translations render Harvey's meaning accurately, as indeed they do with slight exceptions, the form and language become, what indeed they are, matters of taste. There can be no doubt that

both the 1653 version and Leake's are racier than Willis'. Leake has aided comprehension, especially in the longer passages, by breaking them into shorter paragraphs. His translation has the air of easy comprehensibility; he has gone further than those who dressed Shakespeare in modern clothes. But the text of 1653 conveys that feeling of antiqueness which makes it easier to believe that one is listening to Harvey himself, to the very flavor of the language to which his tongue gave utterance. But it would be a pity to lose Willis from our taste and company; "the dull excellence of the Victorian text" conveys a singular sense of leisure and devotion with which the world is coming rapidly to part company, but without which a certain pleasure in the thing itself may disappear and so leave to us only knowledge and utility. What matter if the English of Willis is "pompous and verbose;" it is a language of good temper and kindly scholarship. Its leisureliness reflects the deep and quiet interest in Harvey which bore his great admirer onto the completion of his task through the vicissitudes of a laborious life. This reviewer, for one, would unwillingly miss the orotund Willis from the trio of his translators.

Of the footnotes which Professor Leake has added to Harvey's text, good only may be said; they are helpful and many are interesting. More rather than fewer would have been welcome. Harvey touched on so many aspects of the behavior of the heart and circulation which a later time has developed that he distinctly benefits from treatment of this kind.

At the present time it is still unknown whether the addresses which were made at the numerous functions which took place in London under the auspices of the Royal College of Physicians are to be published. It was a distinguished gathering in the course of which interesting material relating to Harvey, his work and his time must come to light. Nor would one willingly let pass into oblivion the film reproducing Harvey's original experiments, which Lewis and Dale prepared for the occasion.

Truly of Harvey it may be said as it can be said of few men, that the fame which he won so promptly in his own life, has grown apace through the centuries and is still undimmed. A. C.

PRACTICAL SURGERY OF THE ABDOMEN. By GEORGE H. JUILLY, M.D., Chief Surgeon to the French Hospital, San Francisco, Calif. 2 volumes. Pp. 1275; 1291 illustrations. Philadelphia: F. A. Davis Company, 1928. Price, $16.00.

IN presenting this result of six years labor, the author has two aims. He first, by means of sketches and notes, attempts to refresh

the memory regarding little anatomical factors of surgical importance which are essential to perfect technique. Second, he lays especial emphasis on diagnosis. This is very important for only thus is one prepared to meet the conditions as they arise or by mistake in diagnosis he may learn much to the advantage of himself and patient.

Before being a good technical surgeon, he should be a good doctor, for many diagnoses are medical and it behooves the surgeon to prepare himself to prevent such mistakes.

The book is a wonderful one of its kind which is not a very common one. It is a great aid in anatomy, diagnosis and technical surgery. It is thoroughly and cleverly illustrated and written in a pleasing style. E. E.

GREFFE OVARIENNE ET ACTION ENDOCRINE DE L'OVAIRE, ÉTUDE HISTOLOGIQUE, BIOLOGIQUE, CLINIQUE, ET CHIRURGICAL. By VITTORIO PETTINARI. Pp. 487; 181 illustrations. Paris: Gaston Doin & Cie, 1928. Price, 70 fr.

THIS monograph is an account of the author's experiments, which consisted of transplanting ovaries into 332 animals, using autoplastic, homoplastic, and heteroplastic ovarian grafts in normal animals of different ages, in females with one or both ovaries removed and in males with one or both testes removed. He studied the histologic changes resulting in the grafts, and the physiologic and morphologic changes resulting in the hosts.

It is difficult to estimate critically the value of this work, as the detailed protocols of the experiments are not given.

He reviews the literature on grafting, and discusses the indications and contraindications of grafting ovaries of monkeys into human individuals, the rôle of the ovary in various menstrual and sexual disturbances, and the technique of grafting. Although work on the physiology of the ovary, and the source and action of the ovarian hormone is reviewed, it is surprising that there is scarcely any mention of recent important American work in this field. I. Z.

LABORATORY MANUAL OF PHYSIOLOGICAL CHEMISTRY. By MEYER BODANSKY and MARION S. FAY. Pp. 234; 9 illustrations. New York: John Wiley & Sons, 1928. Price, $2.00. This manual is a cloth bound, 230-page work, similar in binding and general make-up to Bodansky's recently published Introduction to Physiological Chemistry which it is designed to accompany.

THE authors, in their choice of material for the laboratory course, emphasize the use of quantitative procedures in physiological

chemistry. The qualitative aspects and the preparation of biological compounds, while not neglected, are given a subordinate position. With full appreciation of the value of the student having a quantitative approach to problems of biological chemistry, it seems to the reviewer that in the manual, too much space has been devoted to giving the student the detailed technique of many methods of blood and urine analysis. Many of these methods are continually being modified or superceded by others.

Very complete references to original sources or larger textbooks are given for many experiments as footnotes. This is an unusual feature in a manual to be used by first year medical students and should be particularly valuable, at least to the instructor or advanced student who uses the manual.

Blank papers are inserted throughout the book for the recording of observations or additional directions. An appendix contains a table or logarithms, the composition of buffer solutions and several pages of coördinate paper. A subject and author index and a table of atomic weights complete a very well-written book and one which seems free from typographical errors. F. C.

ASTHMA, ITS DIAGNOSIS AND TREATMENT. By WILLIAM S. THOMAS, M.D., Associate Attending Physician in Immunology, St. Luke's Hospital, New York. Pp. 279; 26 illustrations. New York: Paul B. Hoeber, Inc., 1928.

WHILE Doctor Thomas has given much of clinical value in what he styles "a practical guide to the management of asthma patients," his book is in the main rather disappointing. One who buys a book on asthma has a right to expect a fairly complete treatise on the subject: here he will find merely an extended "Medical Society Lecture," with emphasis on only certain phases. The chapters on the nature, causes and pathology are particularly sketchy and incomplete; there is no adequate description of the nosology of asthma: its clinical variations, which in practice lead to so much confusion. The arrangement of the material might be improved on: for example, a chapter on "Palliative Treatment of Asthma" is sandwiched between chapters on "Physical Examination" and "Protein Skin Tests." There is given an unusually complete list of references, but to what extent they have been used is not very clear. The book gives the impression of taking up more space than is warranted: unusually large type and wide spacing (less than 250 words to a page); of 279 listed pages, 15 are given to references, 19 to index and 66 are blank! The illustrations are well done.

A. B.

FASCIAL GRAFTING IN PRINCIPLE AND PRACTICE. By H. C. ORRIN, O.B.E., F.R.C.S. (EDIN.) Pp. 92; 21 illustrations. Edinburgh: Oliver and Boyd, 1928. Price, 7 s., 6 d.

THE author has presented his work on this subject at a very opportune time. Plastic surgery is advancing in leaps and bounds, not only by reason of the increased number of surgeons employing it but also due to the ever widening field of its usefulness.

The fascia lata is as frequently used for replacements as any other tissue, and this short work gives to the reader the most recent information available upon the subject. It is true that the data is obtained practically from the experience of the writer, yet his experience in the World War and subsequently has rendered him capable of speaking with authority. E. E.

INFANCY AND HUMAN GROWTH. By ARNOLD GESELL, PH.D., M.D., Director, Yale Psycho-Clinic and Professor of Child Hygiene. Pp. 418; with numerous illustrations, charts and tables. New York: The Macmillan Company, 1928.

A PART of this work was rendered possible by the Laura Spelman Rockefeller Memorial Fund grant, and its stated purpose is to deal with early human growth at close range.

Ambushed in his ingeniously designed observatory, the scrutinizer was enabled to peer at, and to photograph, the all-unsuspecting infant in his primitive endeavors, so that an intensive study was made of what is termed the "Normative Summary of the One Month Level to the Thirty Month Level."

Where unusual growth complexes have a bearing upon normal mental growth, they are discussed, for instance, as "The Symptoms of Giftedness in Infancy" and "Pseudodevelopmental Aspects of Mongolism, Puberty Precox, Thyroid Deficiency and Rickets."

The enthusiasm shown in this detailed study of the infantile period is refreshing, but its scientific value is not enhanced by the fondness displayed for fantastic phraseology and the passion for such unusual words as "fixated," "unidextrality," "contraclockwise," and so forth. N. Y.

THE PRINCIPLES OF ANTENATAL AND POSTNATAL CHILD HYGIENE. By W. M. FELDMAN, Senior Physician to St. Mary's Hospital for Women and Children. Pp. 687; 175 illustrations. London: John Bale, Sons & Danielsson, 1927. Price, $7.00.

IN this book the author has fulfilled his purpose of giving to the "educated and thoughtful person, lay or professional," a comprehensive volume on the welfare of the child. He begins with ante-

conceptional hygiene, discussing the important, but too often undervalued influence of heredity on the welfare of the child. Next he considers postconceptional or intrauterine hygiene and, last, postnatal hygiene under which he includes the neonatal, infant and childhood stages.

Much of the subject matter has been presented before, but never in so compact and comprehensive a manner. The author traces each phase of child hygiene from its earliest historical background through the various stages of development to the present time.

The book is so simply written that much of it may be read to advantage by the intelligent lay student of child welfare; but, even though it is not highly technical, it is so scientifically written that it will attract and stimulate every progressive physician interested in the physical, mental and social aspects of child health.

The pediatrician, obstetrician, educator, eugenist, infant mortality statistician, all may read this book with profit and interest. The teacher of pediatrics will find in the volume not only the data which his students should know, but a fascinating method of presentation which makes the student interested in the data. E. B.

SYSTEMIC INFECTIONS. By A. KNYVETT GORDON, M.B., B.C., B.A., Medical Superintendent, Virol Pathologic Research Laboratories. Pp. 176; 7 illustrations. New York: William Wood & Co., 1928. Price, $4.00.

THIS work represents an attempt to encompass a discussion of an extensive subject and its ramifications in a small volume. The result is not very satisfactory. The first part contains a discussion of the theoretical aspects of bacterial infection, and briefly mentions the technique of the collection of material and hematologic methods. The second part deals with infections in the various systems and includes a discussion of therapy. The treatment of the subject is sketchy, and some of the author's statements seem open to question. It is not a noteworthy contribution to the literature.

E. R.

BOOKS RECEIVED.

New Books.

*Criteria for the Classification and Diagnosis of Heart Disease.** By a Committee, JOSEPH H. BARNTON, M.D., ROBERT L. LEVY, M.D., WILLIAM C. MUNLY, M.D., and HAROLD E. B. PARDEE, M.D., Chairman, appointed by the Heart Committee of the New York Tuberculosis and Health Association, Inc. Pp. 92. New York: Paul B. Hoeber, Inc., 1928. Price, $1.50.

*Serum Diagnosis by Complement Fixation.** By JOHN A. KOLMER, M.S., M.D., DR.PH. Pp. 583; 65 illustrations. Philadelphia: Lea & Febiger, 1928. Price, $7.00.

The Medical Clinics of North America. September, 1928, Vol. XII, No. 2. Nebraska University Number. Pp. 254; 40 illustrations. Philadelphia: W. B. Saunders Company, 1928.

*Les Associations Microbiennes Leurs Applications Therapeutiques.** By G. PAPACOSTAS and J. GATE. Pp. 431. Paris: Gaston Doin et Cie, 1928. Price, about $0.75.

*Physical Education Activities of High School Girls.** By the STAFF OF THE DEPARTMENT OF PHYSICAL EDUCATION FOR WOMEN, UNIVERSITY OF MICHIGAN. Pp. 322; 54 illustrations. Philadelphia: Lea & Febiger, 1928. Price, $3.50.

*The Truth About Mind Cure.** By WILLIAM S. SADLER, M.D. Pp. 206. Chicago: A. C. McClurg & Co., 1928. Price, $2.00.

*A Short History of Medicine.** By CHARLES SINGER, M.A., M.D., D.LIT. Pp. 368; 142 illustrations. New York: Oxford University Press, American Branch, 1928. Price, $3.00.

Surgical Clinics of North America. October, 1928, Vol. VIII, No. 5. New York Number. Pp. 293; 141 illustrations. Philadelphia: W. B. Saunders Company, 1928.

*Laboratory Diagnosis and Experimental Methods in Tuberculosis.** By HENRY STUART WILLIS. Pp. 330; 25 illustrations. Springfield, Ill.: Charles B. Thomas, 1928.

*A Laboratory Manual of Physiological Chemistry.** By D. WRIGHT WILSON. Pp. 272. Baltimore: William & Wilkins Company, 1928. Price, $3.50.

New Editions.

Rules for Recovery from Pulmonary Tuberculosis. By LAWRASON BROWN. Fifth edtion. Pp. 244. Philadelphia: Lea & Febiger, 1928. Price, $1.50.

It is always a great satisfaction to have an authority on a technical and specialized subject present it in a simple fashion. This deservedly popular little book appears with several new chapters added. Many changes have been made throughout to keep it abreast of modern knowledge.

Ultraviolet Rays in the Treatment and Cure of Disease. By PERCY HALL, M.R.C.S. (ENG.), L.R.C.P. (LOND.). Third edition. Pp. 236; 63 illustrations. St. Louis: C. V. Mosby Company, 1928. Price, $4.50.

A good statement from the English point of view of a rapidly changing but important subject.

Bacteriology. By ARTHUR ISAAC KENDALL, B.S., PH.D. Third edition. Pp. 733; 111 illustrations. Philadelphia: Lea & Febiger, 1928. Price, $7.00.

Notable recent contributions included in this edition are the Kahn test, studies on scarlet fever, filterable viruses, bacteriophage, etc. The new alternative nomenclature is not included.

*A Textbook of Pathology.** By WILLIAM C. MACCALLUM, M.D. Fourth edition. Pp. 1177; 606 illustrations. Philadelphia: W. B. Saunders Company, 1928. Price, $10.00.

* Reviews of titles followed by an asterisk will appear in a later number.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

JOHN H. MUSSER, M.D.,

PROFESSOR OF MEDICINE, TULANE UNIVERSITY OF LOUISIANA, NEW ORLEANS.

The Heart in Infection.—"Heart disease is rarely an affection of the heart exclusively, but rather only a part of a general systemic malady. In both its anatomy and physiology the heart has unique features which require consideration, but too close attention to them without due regard to the general problems of the biology of infection and degeneration may have a deterring rather than a beneficial effect." SWIFT (*Am. Heart J.*, 1928, **3**, 629) in this comprehensive and thoughtful paragraph, opens his broad review on the reaction of the heart to the several infectious diseases that he takes up in some detail. Diphtheria represents a disease in which the cardiac injury is dependent solely upon the diphtheritic toxin, producing degeneration of the muscle fibers at first, followed rapidly by interstitial response. In no other infectious disease, except rheumatic fever, is the conduction system so extensively involved, as shown by electrocardiograms. A feature of the diphtheritic heart is the small amount of residual crippling despite extreme functional disturbance at the time of the acute attack. Scarlet fever illustrates the several types of cardiac lesions resulting from infection better than any other single disease. These may be classified as: (1) toxic; (2) allergic; (3) septicopyemic. The toxic type is comparable to the disturbances produced by diphtheria and is practically never fatal. The allergic form is represented by verrucous endocarditis. It may well be that the allergic phenomena occurring late in the disease are induced in part at least by a preëxisting streptococcal hypersensitiveness. The myocardium exhibits a histopathologic picture more closely resembling rheumatic fever than in any other disease. The extremely rare septicopyemic type of cardiac complication is analogous to other forms of malignant endocarditis. As is to be anticipated from the interest of the author in rheumatic fever, the longest section of the review is

devoted to this disease. He discusses briefly not only the Aschoff body and the production of verrucous endocarditis but elaborates conconsiderably on the theme that allergic phenomena are responsible for the lesions of rheumatic fever, theorizing in part as to the manner the endo- and myocardial lesions are produced and concluding that the disease may be said to be a disease of visceral bloodvessels primarily. Subacute bacterial endocarditis may be said to be an example of difference in reaction of tissue to noxous stimuli. Syphilis represents a disease in which allergy is responsible for the luetic lesions. Without the development of an allergic state, spirochetes may lie dormant in the body until cellular reactivity is altered. In septicopyemia severe intoxication and cachexia are more responsible for death than is the ulceration of the valvular tissue. The rôle of toxins in playing a part in the manifestation of cardiac injury is still an open question. No matter whether the hypothetical poison is responsible, or the call on the heart for extra work, or both, the fact remains that such hearts show the usual response to digitalis. Concluding his article, Swift writes that he does not wish to leave the impression that any single type of cardiac infection includes only one type of tissue response; such is far from the case.

Some Observations of Intestinal Amebiasis Due to Infection with Entamœba Histolytica.—James (*Ann. Int. Med.*, 1928, **2**, 171) writes that in the small precystic and cyst-forming stages Entamœba histolytica is hard to find and so difficult is their differentiation from Entamœba coli, Endamœba nana and Iodamœba butschlii that it is possible only for a trained protozoölogist to make the diagnosis of intestinal amebiasis, unassociated with dysentery, from the examination of fresh material. However, one less skilled than the rare and exceptional expert may successfully determine the presence of these parasites, and separate the four species by making wet fixed or permanent dry-stained preparations. In this article of James he discusses other phases of amebiasis based on an intensive study of the disease for the past twenty years. He instances the fact that only recently has it been known that amebiasis without dysentery may produce extensive damage to the mucous membrane of the large gut without diarrhea and without readily visible gross change. Furthermore, while some parasitologists insist that histolytica is always a true parasite, it seems quite possible that the organism may live normally in the upper bowel and it invades the tissues only under certain conditions. Under any circumstance, this should not be construed as a reason for not attempting to eradicate the organisms, potentially an enemy to the host. Fortunately the human host has a relative immunity to the infection, as evidenced by the rarity with which ulceration goes on to perforation. It would seem likely that secondary bacterial invaders are as responsible as the amebæ for the extensive lesions. On the other hand, there is the possibility that a lytic ferment, latent in the organisms, may become activated under certain stimuli, producing extensive tissue destruction, as seen in the so-called sterile abscesses of liver and brain. James writes that this is borne out by the marked *early* congestion and thrombosis of the terminal vessels of the circulatory system, which occurs before any mechanical factor can be concerned or bacterial infection has occurred.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY, SCHOOL OF MEDICINE AND ASSOCIATE PROFESSOR OF SURGERY, GRADUATE SCHOOL OF MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS.

Surgery of the Large Intestines.—POOL and GOVERN (*Am. J. Surg.* 1928, **4**, 245) state that a careful study should be made even before the relatively innocuous operation of appendectomy, lest tuberculosis or carcinoma of the colon, inflammation of Meckel's diverticulum, a ureteral stone, disease of the gall bladder or duodenal ulcer—the real cause of the symptoms—be overlooked. Most lesions of the large intestines, not including the rectum, are situated in the cecum and must be considered as possibilities in the study of the average case presenting abdominal symptoms. The authors review these possibilities. The most frequent sites of localized tuberculosis are the cecum and ascending colon, though any part may be affected. The hyperplastic type is the most significant to the surgeon. This is a slow chronic development with marked thickening of the intestinal walls and relatively little ulceration. The symptoms suggest chronic intestinal obstruction. In general, tuberculosis of the colon should be treated conservatively. It has been shown notably by Lawrason Brown that intestinal tuberculosis can heal completely. Actinomycosis occasionally reaches the tissues from the intestinal tract. It grows in characteristic fashion as colonies of yellowish granules, presenting under the microscope radiating filaments. The ileocecal region is the usual site. A fistula finally develops with extensive infiltration. The operation of resection is then useless. The colon is a frequent and relatively favorable site of cancer, because the neoplasm ordinarily is limited in extent, slow in growth and late in metastasizing. Moreover, metastases are for a long time confined to the regional lymph nodes and these can be excised with the growth. Late recognition is the rule, although there are usually suggestive clinical features—blood in the stools, abdominal discomfort and derangement of the bowels. In the right colon, diarrhea usually occurs for a time, whereas progressive constipation is associated with cancer of the left colon. Mesenteric obstruction; Hirschsprungs's disease, amœbic dysentery and polyposis are touched upon also.

Posterior Mediastinal Abscess following Suppurative Arthritis of Cervical Vertebra.—WAGNER (*Ann. Surg.*, 1928, **87**, 511) believes that mediastinal suppuration are rare, but when present are very serious complications and most often fatal. There is hardly any chest condition which so tests the acuity of the diagnostician. The interpretation

of the reference of pain and the Roentgen ray findings is often extremely difficult. The diagnosis can always be settled by the exploratory puncture of the mediastinal cavity associated with a thorough roentgenologic examination of the thorax. The ideal treatment of course as soon as the diagnosis is established, is surgical. Guadianii has classified the cases in an excellent article as follows: "The abscess which gravitates not lower than the fifth dorsal vertebra can be successfully drained by a cervical mediastinotomy, while all others should be approached by rib resection through the dorsal route."

Treatment of Ulcer of the Stomach and Duodenum.—De Courcy (*Ann. Surg.*, 1928, **87**, 566) says that while focal infection undoubtedly occupies a definite rôle in the etiology of gastric and duodenal ulcer, we must not overlook the important part played by the daily abuse of the stomach. Peptic ulcers may be classified as ulcers of the mucosa or submucosa, ulcer of the entire wall, indurated ulcer and delaminating ulcer with or without induration. A new operation for treatment of the submucosal ulcers is described. It consists essentially in gastroenterostomy, plus cauterization of the ulcer from within the stomach. It is possible that gastrojejunal ulcers following posterior gastroenterostomy are due to contact infections from the original ulcer as in the case of the kissing ulcers described by Moynihan. The ultimate operation for indurated ulcers, particularly in older patients, will be partial gastrectomy. Careless closure of the duodenum is an important factor in the mortality. In patients under thirty years of age, medical treatment should be given a thorough trial before operation is advised.

Early Diagnosis of Intussusception in Children.—Shannon (*Minn. Med.*, 1928, **11**, 221) states that successful treatment is dependent more upon an early diagnosis than upon any other factor, provided reasonably skillful surgery is employed. Intussusception is an invagination of the bowel itself. It consists of two portions, that portion of the bowel which is intussuscepted, the so-called intussusceptum and that portion of the bowel into which the intussusception occurs, the so-called intussuscipiens. Intussusception almost universally takes place in a downward direction. Strangulation of the intussusception rapidly occurs, with interference with the blood supply and thrombosis of the blood-vessels. This leads rapidly to gangrene, a condition which is highly fatal in tiny babies. The intussusception may occur in the small bowel, in the large bowel, or at the ileocecal valve. This last variety is the commonest. The cardinal points of early intussusception are pain, sudden and severe, first constant, later intermittent; early nausea and vomiting (in 166 cases out of 170, according to Hess); prostration, sudden and out of proportion to other symptoms; tumor, the most important sign, present in over a half of the cases; stools which contain blood in varying amounts after one or more normal evacuations; temperature which is typically absent or subnormal in early stages. In an analysis of case reports, the author shows that all of the cardinal points have been violated in one or more instances.

THERAPEUTICS

UNDER THE CHARGE OF

CARY EGGLESTON, M.D.,

ASSISTANT PROFESSOR OF CLINICAL MEDICINE, CORNELL UNIVERSITY MEDICAL COLLEGE, NEW YORK CITY.

Experimental Studies on the Actions of Synthalin.—H. STAUB presents (*Ztschr. f. klin. Med.*, 1928, **107**, 607) the results of an extensive series of investigations made to determine the precise nature of the actions of Frank's synthalin and the structures in the body upon which they are exerted. It is his prime purpose to determine whether synthalin is a true substitute for insulin. He finds that the initial effect of the parenteral administration of synthalin to normal animals is the appearance of a hyperglycemia. After a period of from six to ten hours hypoglycemia makes its first appearance. This is quite different from the action of insulin in which reduction of the blood sugar begins to take place immediately. Further the doses of synthalin necessary to produce hypoglycemia are highly toxic and their toxic and even fatal actions cannot be prevented by the administration of sugar as in the case of insulin. The toxic actions which appear are always those of guanidin poisoning. His experiments show that the chemical changes in the guanidin molecule which give rise to synthalin lead to a general increase in guanidin action, both the blood sugar lowering action and the neurotropic actions being enhanced. The respiratory center is first stimulated and then paralyzed by synthalin. The hyperglycemia appears to be due to an action on the sympathetic nervous system. Synthalin exerts a direct toxic action on the liver and produces degeneration and a fat deposit. The liver is the chief organ in the body which exerts a detoxifying action upon this agent. Vagotomy exerts no influence upon the synthalin action on blood sugar. The initial hyperglycemia can be proved experimentally to be due to a stimulation of the sympathetic system similar to that produced by adrenalin, and secondarily glycogenolytic action synthalin takes place directly upon the liver occurring in the perfused organ. Following the administration of synthalin there is a diminution in oxygen consumption and there is a marked change in the amino-acid metabolism in the liver. It appears also that the synthesis of sugar from protein is diminished. The site of action at which synthalin produces hypoglycemia appears to be peripheral in the tissues of the body musculature. The author concludes from his careful metabolic studies that the reduction of blood sugar is due to an anoxybiotic process by which a considerable proportion of glucose or glycogen is convered into lactic acid. Synthalin primarily diminishes the oxygen respiration of the tissues thus giving rise to this anërobic production of lactic acid. Synthalin is easily demonstrated to be a cell poison inhibiting the growth of bacteria and the lipase fermenting power of the serum and of the pancreas. It is obvious from the results of this investigation that the actions of synthalin are totally different from those of insulin and that it is in no sense a substitute for the latter agent.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.,
OF PHILADELPHIA.

Diseases of Children Benefited by Splenectomy.—KENNEDY (*J. Am. Med. Assn.*, 1928, **91**, 874) presents this paper for the purpose of reviewing the diagnostic methods employed and the results of the treatment of those diseases in children for which splenectomy is performed. In the Mayo Clinic, splenectomy was performed for hemolytic icterus on 17 children. All recovered from the operation. One patient died later from other causes. The test of the fragility of the erythrocytes seemed to be the most useful criterion in diagnosing hemolytic icterus. It was found to be increased in all cases and after the operation it did not return to normal. Ten children with purpuric manifestations were operated upon. All recovered from the splenectomy. One patient some weeks later died from hemorrhage following tonsillectomy. One patient showed a normal platelet count, one patient showed the characteristics of hemophilia, hemorrhagic purpura and aplastic anemia, and one, who died after tonsillectomy, showed the picture of aplastic anemia. Kennedy feels that there is still considerable doubt as to the exact significance of the platelet count in diagnosis. Splenectomy was done in 7 cases of splenic anemia. All recovered from the operation, but 3 died later from other causes. At one operation a chronic inflammatory condition was found and was classified as chronic infectious splenitis. The diagnosis of splenic anemia covers a heterogenous group of conditions in which anemia, leukopenia and splenomegaly are present. It is hoped that better groups of classification will be evolved. One case observed in this study presented puzzling features, but it was found to be chronic infectious splenitis with secondary cirrhosis of the liver. It seems probable that early splenectomy in certain conditions will prevent progress and in some cases will result in decrease of the secondary cirrhosis of the liver. On study of the spleens histologically no characteristic changes of the particular diseases were observed.

Cardiac Symptoms in Scarlet Fever.—REINHARD (*Arch. f. Kindh.*, 1928, **84**, 210) observed 160 children during the entire six weeks of the scarlet fever. He found the heart involved in 84. This involvement consisted of a soft systolic noise over the apex, and it often was so slight as hardly to deserve the term of murmur. Reinhard feels that the term "impurity" describes it better. Accentuation or splitting of the second sounds, usually of the second pulmonary, was noted. There is sometimes a slight enlargement of the heart to the left. The pulse is often irregular. Usually there are no subjective symptoms. In 19 of the children the symptoms were present on admission on the second day or the third day of illness. In 36 of the children the symptoms appeared between the fifth and twenty-fifth days, in 4 in the fifth week,

and in 2 in the sixth week. In 4 children the time of the onset of the cardiac symptoms was not noted. There were only 10 in whom the symptoms cleared up within two or three weeks, but in 24 they had cleared up entirely in six weeks. There were 60 children who left the hospital with cardiac symptoms. Opportunity to examine 35 of these was offered in from three weeks to four months after their discharge. The heart symptoms had entirely disappeared in 13. Eleven showed improvement. Three children whose scarlet fever dated from earlier periods were examined six and a half, nine and a half and nine months after their discharge. In these children the murmur described had been noted during their illness, and it was still distinctly noticeable. "Scarlet fever heart" does not seem to be dependent on the severity of the scarlet fever infection, or is it related to rheumatism or nephritis. Of the 160 children observed during this study only one developed an endocarditis. The author feels that the condition is a slight degenerative process in the myocardium.

Knoepfelmacher's Modified Butter-meal in Infant Feeding.—JUNGWIRTH (*Monatschr. f. Kindh.*, 1928, **38**, 500) presents his results in 55 cases in which he used this concentrated feeding. This has the highest caloric value of the butter-meal combinations, 100 gm. affording 260 calories. In 40 of 55 cases of dystrophy following dyspepsia, pylorospasm, atrophy, persistent vomiting, premature birth, syphilis, whooping cough, pneumonia, tuberculosis and rickets good results were obtained. The Knoepfelmacher formula is 130 gm. of milk, 10 gm. of flour, 10 gm. of butter and 15 gm. of sugar boiled down to 100 gm. The high-calorie content makes it possible to obtain a rapid increase in weight during the convalescent period in undernourished children, and supplies an adequate amount of energy for combating dystrophy. The food is contraindicated where there is difficulty in swallowing the thick meal, in dyspepsia and intoxication, and in infants less than two or three months of age.

The Rôle of Streptococci in Experimental Poliomyelitis of the Monkey.—LONG, OLITSKY and STEWART (*J. Exper. Med.*, 1928, **48**, 431) were unable to determine that there existed any etiologic relationship between the streptococci recovered from poliomyelitic tissues and poliomyelitis. The fermentation reactions of the microörganisms obtained from the air and from nonpoliomyelitic and poliomeylitic monkey brains suggest that bacteria from any of these sources are markedly different. Similar indications arise from the reactions of agglutination and precipitation. They observed no agglutination when the serum of monkeys convalescent from experimental poliomyelitis was mixed with any of the streptococci recovered or those received directly or indirectly from Rosenow. The intracerebral injections with cultures, irrespective of their source, induced in rabbits a purulent type of meningoencephalitis, often associated with streptococcic septicemia. This result was at marked variance with any known effects of the true filtrable virus of poliomyelitis in man or monkey.

Chronic Splenomegaly in Childhood.—HUTCHINSON (*Brit. Med. J.*, 1928, ii, 281) emphasizes the rôle played by syphilis and rickets in the production of chronic splenomegaly. Splenic enlargement is often associated with an idiopathic cirrhosis of the liver and this picture must be differentiated from Banti's disease. Biliary cirrhosis is often associated with splenomegaly. Splenic thrombosis is often the cause of enlarged spleen. Splenic anemia of the adult type followed by Banti's disease may occur and be the factor responsible for the splenic enlargement. Therapeutically those cases suitable for operation by splenectomy are those which show a negative Wassermann reaction, no enlargement of the lymph glands, and no characteristic leukocytic picture, but in which there is a certain degree of anemia associated with leukemia, increased fragility of the red cells, or hematemesis.

DERMATOLOGY AND SYPHILIS

UNDER THE CHARGE OF

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AND

STANLEY O. CHAMBERS, M.D.,

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Traumatic Alopecia Areata. MONTIER and LEGRAIN (*Ann. d. dermat. et d. syph.*, 1928, **9**, 268). **The Physiopathologic Mechanism of Alopecia Areata.**—FRANKEL and JUSTER (*Ann. d. dermat. et d. syph.*, 1928, **9**, 285). These two articles support strongly the conception of alopecia as due to a lesion of the sympathetic nervous system or its associated endocrine and vasomotor mechanisms. Montier and Legrain describe a series of cases drawn from war experience of alopecia areata following trauma to head and face, with nerve injuries and without Roentgen ray intervention. The known association of ophthalmic zoster with such lesions is cited. Frankel and Juster discuss the concomitant findings in alopecia areata which suggest a lesion of the sympathetic nervous system. It is stated, though no figures are given to support the assertion, that disturbances of oculocardiac, pilomotor and nasofacial reflexes are frequent in the subjects of alopecia areata; that abnormalities of sweat secretion and local edema and vasomotor changes may occur at onset and disappear on recovery from the alopecia; that increased basal metabolism occurred in 18 of 25 cases and decreased in 5. Capillary microscopy in one subject by the methods of A. C. Guillaume indicated a spasm of the arterioles throughout the patch, with accentuation at the periphery of the lesion with accompanying symptoms of a disturbed sympathetic mechanism. The authors disclaim any intention of classifying all cases of alopecia areata on a single pathologic mechanism.

GYNECOLOGY AND OBSTETRICS

UNDER THE CHARGE OF
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AND
FRANK B. BLOCK, M.D.,
ASSOCIATE IN GYNECOLOGY, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Cystoscopy Reactions.—In the present-day practice of gynecology the employment of cystoscopic examinations has become well nigh indispensable. When we advise this type of examination there are two questions which patients are prone to ask, namely, "Will it hurt?" and "Is there any danger?" To the first question we can usually answer in the negative, thanks to the easily distensible female urethra and also the use of local anesthesia in some cases. As to the second question it must be admitted that occasionally there are some reactions of varying intensity, although seldom of dangerous proportions. This subject has been investigated by WEHRBEIN (*Ann. Surg.*, 1928, **87**, 435), who analyzed over 300 cystoscopic examinations which were done at the Bellevue Hospital in New York. He found that reactions are rarer in women than in men and as a result of his study he came to the conclusion that they are largely due to infection and trauma. It is quite possible that infection *per se* might set up a febrile reaction, but trauma seems to be such a strong contributory factory that it should be given almost equal weight. He cautions that the utmost gentleness and accuracy should be exhibited by the cystoscopist and the instrument used should be of the smallest caliber that will permit a satisfactory examination.

Complications Following Irradiation of Pelvic Lesions.—While all gynecologists of experience will unhesitatingly concede that radium is a most valuable therapeutic measure when properly used, they will also admit that when used in the presence of certain contraindications it may be productive of complications, which at times may lead to a fatal issue. In order to reduce the incidence of these complications to a minimum, STACY (*Am. J. Roentgenol.*, 1928, **19**, 323) states that in her department at the Mayo Clinic a thorough physical examination is imperative, including a cystoscopic examination when bladder irritation exists, before radium treatment is instituted in cases of carcinoma of the cervix. Great improvement in the local condition often follows the use of a few short periods of irradiation at intervals of several days in cases of extensive malignancy in toxic patients. This is in contrast to the severe reaction which is sometimes seen when a large dose of irradiation is given at one time in patients of this type. When evidence of pelvic infection occurs treatment should be discontinued until all signs and symptoms of infection have subsided, while if the patient's

condition is not good the treatment should be abandoned. Tissue reaction with slow healing, at times difficult to differentiate from an extension of the malignancy, may occur in the vesical or rectal mucosa, producing local symptoms many months after the use of radium. In one year at the Mayo Clinic complications developed after radium treatment in about 18 per cent of the cases of carcinoma of the cervix but only in 2.2 per cent of the cases of benign disease.

OTO-RHINO-LARYNGOLOGY

UNDER THE CHARGE OF

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Nutritional Edema and its Relation to the Incidence of Common Colds.—It is established that edema can result from a variety of causes, notably impairment of circulatory or renal function, and nutritional disturbances such as excessive salt and vegetable intake or deficiency in vitamins or fat. In a most instructive report, HOELZEL (*Proc. Soc. Exper. Biol. and Med.*, 1928, **25**, 454) describes a type of nutritional hydration in which protein starvation was the primary factor. However, the gross manifestation of nutritional edema seemed to be possible only when the diet contained sufficient salt or carbohydrate or both. As nutritional edema, in mild form, seemed to be very common, often following illness associated with undernutrition, a consideration of the possible relation of such edema to other common complaints naturally suggested itself. In this regard, the author has observed a close parallelism between the incidence of colds and nutritional hydration. Colds were never caught during prolonged fasting or marked and prolonged undernutrition. They developed almost invariably after such periods when edema was also most prominent. Distinct colds have been prevented by keeping the hydration of the organism at a relatively low level, mainly by restricting the carbohydrate intake and maintaining an adequate protein intake. In the light of these observations, colds are regarded as a common consequence of a chilling of highly hydrated and sensitive skin, with the result that an overload of fluid is thrown upon already hydrated internal structures, including the upper respiratory tract. Bacteria may then play a complicating rôle after excessive secretions have thus been established.

Autosterilizing Power of the Nasal Mucous Membrane.—By taking swab cultures at various time intervals from the nares of guinea pigs, rabbits, dogs and human beings, into which living bacteria had been sprayed, ARNOLD, OSTROM and SINGER (*Proc. Soc. Exper. Biol. and Med.*, 1928, **25**, 624) found that 90 to 95 per cent of the viable organisms were rendered nonviable within five to ten minutes. An average of

400 experiments were conducted on 42 normal human beings, and 185 experiments on the different animals. Repeated application of bacteria to the nasal mucosa was not associated with an exhaustion of this disinfecting mechanism. Cultures obtained from bacteria which had survived the initial period of the disinfecting action were removed from the nasal lining as promptly as the original strain. Repeated applications did not lead to the development of a resistant strain. No growth—inhibiting substance could be demonstrated in the nasal washings and secretions *in vitro*. Subjects in warm rooms showed a retardation in the disappearance of the microörganisms from the nasal mucosa. B. prodigiosus and B. coli were found to be the most satisfactory bacteria for experimentation, both disappearing in the same ratio.

Pneumococcus Types in Acute Mastoiditis and "Primary" Pneumococcus Meningitis. Preliminary Report.—BAUER and ST. CLAIR (*J. Am. Med. Assn.*, 1928, **90**, 1429) found that in 13 cases of "primary" pneumococcus infection of the mastoid cells, and in 5 of the meninges, in which the organisms were typed, Type III pneumococci predominated in those cases following otitis media and Type IV pneumococci, in meningitis without a history of otitis media. The cases of pneumococcal mastoiditis represented about one-tenth of the cases of mastoiditis from which cultures had been taken over a four-year period.

RADIOLOGY

UNDER THE CHARGE OF

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Use of Amyl Nitrite as an Antispasmodic in the Roentgen Examination of the Gastrointestinal Tract.—Organic lesions of the digestive tract are often simulated roentgenologically by spasm. To relax this spasm an antispasmodic, usually belladonna or atropin, is given for physiologic effect and the patient is then reëxamined. Recently HOLMES and DRESSER (*Am. J. Roent. and Rad. Therap.*, 1928, **19**, 44) have tried amyl nitrite for this purpose. During the course of the usual roentgenoscopic examination the patient is placed recumbent on the table and required to inhale the fumes from one or two "pearls" crushed in a wad of gauze. In a few moments the subject usually complains of throbbing of the temples, slight dizziness, and a warm flushed feeling. Relaxation of spasm occurs at this time, if at all. It has been found useful in the examination of the irritable spastic type of colon and in relax-

ing cardiospasm. Spasm produced by intrinsic lesions of the alimentary tract is apparently unaltered, coinciding in this respect with the effect attributed to atropin. In pylorospasm of presumably extrinsic origin, no relaxation occurred. The writers conclude by expressing the belief that all antispasmodics are unreliable in their effect on the stomach and duodenum and that their value in diagnosis has been overestimated. Discussing this paper, Moore, of Rochester, expressed the opinion that spasm of the stomach and duodenum from extrinsic causes is relatively rare. He thinks that fright and other mental conditions are very important elements in producing spasm of the alimentary tract, and that relaxation after giving belladonna may be due, not to the action of the drug, but to the fact that the patient is not frightened at the second examination. He had never been able to bring about relaxation of cardiospasm by antispasmodics.

Ulceration of the Colon.—Mooney (*Radiology*, 1928, **10**, 29) discusses ulcerative colitis and tuberculous colitis. Ulcerative colitis may be acute and fulminating with severe diarrhea, abundant blood, pus and mucus in the stools, severe abdominal pain, tenesmus, extreme prostration and very often death. Improvement may slowly take place with apparent cure in some cases, but as a rule a train of symptoms persist, such as semiliquid stools containing blood, pus and mucus, and the sigmoidoscope may reveal not only active inflammation of the bowel but also ulcers. In another group the onset is insidious and routine Roentgen ray examinations of the gastrointestinal tract may give the first hint of the real trouble. A twenty-four-hour plate showing the bowel empty or only streaks of the opaque meal remaining in the descending colon should call for a rigid inquiry into the history and a barium enema. The ulceration at first involves the mucous membrane, but gradually invades the deeper layers of the colon, causing abscess formation, which in turn results in fibrous tissue and narrowing of the lumen. The radiographic picture is characteristic. Haustral markings are absent and the barium shadow is narrow and tubelike. In advanced cases localized constrictions at intervals along the narrowed bowel cause it to appear like a string of sausages. The disease usually begins at the rectum and extends toward the cecum, but it may start in any portion of the colon. It is always better to confirm the Roentgen findings by sigmoidoscopic examination and to correlate both with the history. If ulceration of the lower bowel is seen with the sigmoidoscope the diagnosis is confirmed; if beyond reach of the sigmoidoscope, the history, clinical picture and roentgenologic appearance are usually diagnostic. Mooney believes that the disease is not uncommon and that its early stages are frequently overlooked. Tuberculous colitis is of frequent occurrence in tuberculous patients. It is usually confined to the cecum and ascending colon. Spasm, absence of haustration and filling defects are observed roentgenoscopically. The lumen of the bowel is encroached on and the shadow is irregularly narrowed. When the film is developed this part of the bowel may be entirely empty of barium, and this rapid emptying of the affected segment is characteristic of tuberculous ulceration. The radiographic signs coupled with clinical tuberculosis in any other part of the body, particularly the lungs, should make the diagnosis of tuberculous colitis reasonably certain.

Spasticity of the Colon.—Derangements of the colon, according to McMillan (*Radiology*, 1928, **10**, 35) are responsible for many chronic abdominal complaints, and the most common of these derangements is spasm. Spasm of the colon may be local or general. Local spasm generally affects the sigmoidal colonic juncture, or the first part of the transverse colon. The bowel is narrowed in these localities for a variable extent, resembling an annular new growth. That portion of the bowel proximal to the narrowing is usually dilated. If the spasticity is general, the transverse and descending portions of the colon and the sigmoid are usually involved. A diseased appendix, anal or rectal fissure and ulcer have been assigned as possible causes, but McMillan believes that they are not at all common. The marked relief afforded some of these patients by proper dietary measures suggests that errors in diet and habits must constitute a cause. In others, no doubt, some derangement of the nervous control is a contributory factor. Sex and age seem to play but little part, although McMillan feels that it is more common in patients over thirty years of age. Among the symptoms are general abdominal discomfort, pain variously situated but usually following the course of the colon, often coming on during or immediately following the meal, and alternating diarrhea and constipation. For roentgenologic examination both the opaque meal and the enema are of service, but McMillan prefers the former. When all the meal has reached the large bowel, the greater part may be massed in a dilated cecum and ascending colon while the remaining portion of the bowel may be contracted. In the distal portions of the colon the meal is segmented. Subsequent examinations will show even more marked spasticity without any forward movement of the contents of the bowel. With the opaque enema the mixture generally passes through the colon in a small stream and when the colon is completely filled the cecum and ascending colon appear dilated, the rest of the bowel being especially narrowed at the juncture of the descending colon with the sigmoid. Occasionally the descending portion and sigmoid have a "saw-tooth" appearance resembling diverticulosis.

Complications Following the Application of Radium to Pelvic Lesions.—Systemic reactions considered due to acidosis together with pelvic cellulitis, peritonitis and hemorrhage occurring after the use of radium in carcinoma of the cervix and other conditions, are discussed by Stacy (*Am. J. Roent. and Rad. Ther.*, 1928, **19**, 323) from her experience at the Mayo Clinic. Among 134 cases of inoperable carcinoma treated with radium, 24, or 17.9 per cent, developed complications during or immediately after irradiation. In 23 cases of carcinoma of the fundus in which intrauterine radium treatment was given, fever and phlebitis developed in only one. Two hundred and twenty-seven patients were treated during the year for menorrhagia associated with a fibrous type of uterus or with uterine myoma, complications occurring in 5, or 2.2 per cent. Complications can be avoided to some extent by special preliminary care of anemic patients. Patients are likely to withstand the full course of radium better if the first two treatments are light and given several days apart.

Effect of Irradiation on the Suprarenal Gland.—From his own investigations and the work of others DESJARDINS (*Am. J. Roent. and Rad. Ther.*, 1928, **19**, 453) concludes that much of the experimental work bearing on the biologic effect of irradiation of the suprarenal glands is of doubtful value, because it has often been based on unfounded assumptions, and many of the records are full of unwarranted deductions. Experiments on animals show that Roentgen rays may cause pathologic changes in the suprarenal gland, but strong doses, well beyond the therapeutic range, must be used to induce such changes. The pathologic alterations affect chiefly the cortical portion of the gland; medullary changes also may occur, but this portion of the organ is distinctly less susceptible to irradiation than the cortex. In spite of the morphologic disturbances in the suprarenal produced by irradiation under experimental conditions, the health of the animals was not impaired. Since the suprarenal factor influencing blood pressure is chiefly a product of the medullary cells, the ground for the contention that irradiation can diminish blood pressure in hypertension is not solid. This applies also to the theory that irradiation of the suprarenal glands can diminish the blood sugar of diabetics.

Arthritis and the Menopause.—Arthritic complaints are so common at the climacteric that Cecil and Archer have regarded the term "menopause arthritis" as warranted. CORSCADEN (*Am. J. Roent. and Rad. Ther.*, 1028, **19**, 321) has undertaken a study of women in whom a radiotherapeutic menopause has been induced, to determine whether any relation exists between arthritis and this artificial menopause. Sixty cases were studied. Of the 60 women 5, over forty years of age, developed continuing symptoms referable to the joints. In none of the women under forty have there been any persistent joint symptoms. From the evidence it would appear that the abrupt termination of menstruation by radiotherapy has not been an important factor in causing arthritic changes. While there have been some joint manifestations following the induction of the artificial menopause they have been for the most part temporary, and those which have persisted have been of such a varied character that they do not impress one as having a common origin. From the practical standpoint one must regard the relationship between the therapeutic menopause and arthritis as unimportant and must ignore it in deciding upon the merits and demerits of the procedure; in the management of joint conditions, one should minimize efforts directed toward replacing deficient ovaries substance and concentrate on the more conventional methods.

Radium in the Treatment of Cancer of the Cervix Uteri.—WARD (*Am. J. Roent. and Rad. Ther.*, 1928, 19, 330) reports the results in 232 cases treated at Howard A. Kelly Hospital, Baltimore, during 1921–1922. Among the 141 inoperable cases 9 per cent were clinically cured when last seen, and 4 per cent have passed the five-year period as well. Of the operable cases 50 per cent have passed the five-year period with no evidence of recurrence.

NEUROLOGY AND PSYCHIATRY

UNDER THE CHARGE OF

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Malarial Therapy and the Preparetic.—LANG (*Psychiatric Quarterly*, 1928, **2**, 115) in this paper, stresses the importance of early diagnosis of neurosyphilis. He believes that malarial therapy is indicated in all early cases, especially when no improvement can be noted after active antiluetic therapy. According to Wile and Hasley and Cornaz from 22 to 35 per cent of patients with preëxanthematous syphilis show abnormal spinal fluids whereas during the secondary stage, according to Stokes and McFarland and Fordyce and Rosin, the proportion having abnormal spinal fluid mounts to as high as 70 per cent. As a consequence, Lang believes that lumbar puncture is necessary in treatment of all cases of syphilis. He also states that the procedure should be routinely followed in all cases admitted to psychopathic hospitals and cites case histories of typical functional psychoses where the spinal fluid revealed a more serious condition present. Lang gives an excellent outline of the chief and diagnostic characteristics of cerebral syphilis as follows: Multiplicity and transiency of symptoms; early headache, nausea and vertigo; neurologic findings as kaleidoscopic paralyses, tremors, speech disturbances, auditory and visual hallucinations, pupillary anomalies; mental reactions as temporary periods of confusion, listlessness, depression, occasional delirium; serologic findings as weak Wassermann reaction in spinal fluid, variable cell count according to acuteness or chronicity of process, gold curve of luetic type with precipitation in middle tubes, blood Wassermann positive in 50 per cent of cases. The author then proceeds to outline the classical symptoms and physical findings of paresis, stressing the characteristic serologic findings such as paretic gold curve, strongly positive Wassermann reaction, high cell count, and so forth. He believes that malarial therapy can be employed in the home as well as in hospitals but agrees that it is simpler to deal with cases in hospitals where isolation wards can be designated for this purpose.

Cerebral Symptoms Produced by Supratentorial Tumors.—GRANT (*Arch. Neurol. and Psychiat.*, 1928, **20**, 292) analyses 27 cases of mistaken localization occurring in 575 cases in which suboccipital explorations were performed in Dr. Cushing's Clinic. He considers that in these 27 cases the cerebellar symptoms were so prominent as to draw attention away from other localizing signs of positive value. In all

but 6 cases he finds factors such as blindness, uncoöperation, and so forth, which would make the error in diagnosis very difficult to avoid. All of these tumors were supratentorial and were widely distributed throughout the cerebral hemispheres. Thirteen were in the anterior half of the supratentorial space and 14 in the posterior half. Marked increase in intracranial pressure was present in all cases and he thinks the cerebellar symptoms were due to pressure from above. Sixteen of these cases had acute onset with symptoms of pressure. He states that perimetry would have been of localizing value in only 4 of the cases. Roentgen-ray studies proved of little value. He advises in doubtful cases bilateral tap to determine the location and size of the ventricles prior to the operation. As conclusive evidence of supratentorial lesion he would consider discrepancies in size of the ventricles or marked displacement. Nineteen of these 27, he states, could have been localized by this means. If doubt still exists he advises a ventriculogram. He emphasizes the importance of bilateral tap to compare the two sides. "As suboccipital craniectomy in the presence of a supratentorial tumor carries a mortality of approximately four times as great as does this procedure when a subtentorial lesion is present, it is essential to be certain of the position of the tumor before the exploration is attempted." He considers that this series of cases would indicate that differentiation of supratentorial and subtentorial lesions should not ordinarily be difficult.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Filtrable Forms of Bacteria.—A great deal has been written in recent years about filtrable forms of bacteria under the action of bacteriophage and the development of mutation forms from these. FROBISHER (*J. Infect. Dis.*, 1928, **42**, 461) has studied these problems and has shown that many of these forms found in filtrates are environmental bacteria which grow slowly at 37° C., and are therefore usually overlooked. He suggested that the cultural vagaries of secondary growths may often be due to mixtures of the original strain and environmental bacteria. The failure of many authors to use adequate controls explains in his opinion many of the strange findings reported in the literature. He recovered identical organisms from filtrates of sterile broth, bacteriophage-free cultures and bacteriophage cultures of bacteria of entirely different genera and pointed out that secondary growths appear as a

result of the process of filtering and pipetting sterile material. The errors due to obscure defects in the filters or the unnoticed contamination are stressed and he could find no evidence of the occurrence of ultrabacteria due to the action of bacteriophage.

Effects of High-voltage Cathode Rays on the Skin of the Rat.—In view of the extraordinary effects of the cathode rays on various inorganic and organic substances, it seemed of moment to JACOBSON and WADDELL (*Arch. Path. and Lab. Med.*, 1928, **5**, 195), to study thoroughly the effects of the rays on living animal tissue. In order to facilitate the technical procedures, the white rat was chosen as the experimental animal. The intensity of the reaction of the skin varied according to the voltage and the length of the exposure to the cathode rays. The epithelium of the shaved skin is probably killed at once by ten seconds' exposure to 100,000 volt rays. An exposure of one second to 200,000 volts and upward will result in death of the cells of the epidermis. Small doses of cathode rays, such as 0.1 second daily for fourteen days result in degenerative changes in the epidermis. Marked changes occur in the corium, but the bloodvessels are not affected sufficiently to account for necrosis, hence the lesions which develop during a fourteen-day interval are, without much doubt, actual radiation effects. The macroscopic changes noted in the series were, first, an immediate change in color of white hair to yellow. When the hair had been previously removed, a pronounced redness and edema occurred. After forty-eight hours, the skin gradually became leathery and shrunken; it desquamated and an area of necrosis developed at the site of raying, the ulcer never extending in depth farther than the first muscle layer. A thick crust formed, but healing was sluggish and in only one rat was epithelial repair far advanced after fourteen days. The most characteristic lesion of the skin was fusion of the collagen fibers of the corium and necrosis of the epithelium of the skin and hair follicles. Vascular injury is less severe and is most in evidence after hyaline fusion of the collagen appears. In from two to fourteen days, phagocytes and foreign body giant cells appeared around the necrotic cells. The cellular infiltration was most marked in those animals which had received multiple small doses rather than one long exposure. As the cathode rays produce hyaline fusion of the collagen of the corium, and since the characteristic lesion of the Roentgen ray injury is a similar collagen degeneration, the evidence seems conclusive that the biologic effects heretofore ascribed to Roentgen rays, are not due to Roentgen rays, but to the cathode rays which they produce in the tissues.

Pleural Reactions to Tubercle Bacilli.—To obtain an immediate action of the pleura to tubercle bacilli STEINBACH (*Proc. Soc. Exper. Biol. and Med.*, 1928, **25**, 779) found that previous sensitization was necessary. He considered tuberculous pleurisy in guinea pigs to be a reinfection as is believed to be the case in man and as another illustration of the Koch phenomenon which offers advantages for the study of the protective significance of this reaction.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Udder Infection with Streptococci of the Scarlet Fever Type. I. Spontaneous and Experimental Udder Infection.—JONES and LITTLE (*J. Exper. Med.*, 1928, **47**, 945) state that heretofore contamination has been regarded as the usual means of spread of scarlet fever by milk. The findings in regard to septic sore throat, however, indicate that udder infection with the human streptococcus is far more likely. The same may be said of milk-borne epidemics of scarlet fever. The milk of all cows should be promptly investigated when milk-borne infection is suspected, since a few days delay may be sufficient for the disappearance of the streptococcus from the udder. In all the experimental inoculations there was little to arouse suspicion during the first twenty-four hours although streptococci could be readily detected in the milk. After this time abnormalities in the appearance of the milk were apparent. It must be borne in mind that in these experiments the organisms were introduced into the milk cistern, and although the number of streptococci administered was small, in all probability in the spontaneous disease the infective dose would be even smaller; and unless contaminated material was introduced by teat tubes or other means the organisms would probably be deposited at the meatus or about the ends of the teats. This indicates a somewhat longer incubation period than that observed in the experiments. The authors discuss the clinical and bacteriologic findings in two cows the udders of which became infected under natural conditions with hemolytic streptococci of the scarlet-fever type. One of the cows was found in a herd supplying raw milk to a small town where a milk-borne outbreak of scarlet fever had occurred a short time before. When small numbers of the streptococcus obtained from this case were injected into the udder of a normal cow, severe mastitis accompanied by a well-marked general reaction resulted. Evidence leads to the conclusion that a severe attack of mastitis due to this organism in one quarter does not sufficiently immunize the other quarters to protect them completely since the streptococcus can be readily implanted in them. The secondary infections were much milder than the original process. **II. A Study of the Scarlet Fever Type of Streptococci Isolated from the Udder of the Cow.**—JONES and LITTLE (*J. Exper. Med.*, 1928, **47**, 957) have correlated with known scarlet fever strains the streptococcus which they isolated. This streptococcus and another from the udder of a cow are indistinguishable

in cultural characters and certain antigen affinities from Streptococci scarlatinæ. Skin tests indicate that the strain isolated from the milk of the cow in a herd to which the scarlet fever epidemic was attributed produced a toxin which was neutralized with scarlet fever antitoxin.

A Study of the Mechanism of Recovery from Lobar Pneumonia.—SIA, ROBERTSON and WOO (*J. Exper. Med.*, 1928, **48**, 513), employing a method devised for the investigation of natural immunity and experimental pneumococcus infection, made a study of the serum immune changes occurring during the course of lobar pneumonia due to pneumococcus Types I and II and Group IV in man. They found that at the time of crisis or lysis the blood serum acquired constantly the property of promoting pneumococcus killing to a relatively marked degree. Other evidences of antipneumococcus reaction—mouse protection, opsonins and agglutinins—were also demonstrable in the blood at this time. These immune changes appeared in the majority of cases at the beginning of recovery and failed to occur when the disease terminated fatally. The fact that these observations in human cases are practically identical with previous findings in the experimental disease in cats enhances considerably the significance of the development of serum immune bodies at the time of crisis since in the experimental animal it was possible to show that the acquisition of passive immunity was associated with greatly increased antipneumococcus resistance.

A Study of the Blacktongue-preventive Action of 16 Foodstuffs, with Special Reference to the Identity of Blacktongue of Dogs and Pellagra of Man.—GOLDBERGER, WHEELER, LILLIE and ROGERS (*Pub. Health Reps.*, **43**, 1385) report in accordance with the following summary and conclusions: The blacktongue-preventive potency of 16 foodstuffs has been studied and correlated to the pellagra preventive potency (or lack of it) of those, eleven in number, for which this was known, with the following results: *Maize*, if it contains any, is a poor source of the preventive for both blacktongue and pellagra. Whole *wheat* contains the blacktongue preventive, but in small amount. Commercial *wheat germ* contains, and may be rated as a relatively good source of, the preventive for both blacktongue and pellagra. The *cowpea* contains, but is a poor source of, the preventive for both blacktongue and pellagra. The *soy bean* contains the blacktongue preventive, but in relatively small amount, appreciably more, however, than the cowpea, but considerably less than the extracted wheat germ. So far as it goes the experience with the soy bean in the human disease is, at least, not inconsistent with that in the experimental disease of the dog. *Milk* contains the preventive for both the human and the canine disease, but contains it in relatively small amount. *Butter*, while not devoid of it, is a relatively very poor source of the blacktongue preventive, a conclusion that is in harmony with the experience with butter in pellagra. *Cod-liver oil* would seem very poor in or lacking the preventive for both blacktongue and pellagra. *Cottonseed oil* contains little, if any, of the preventive for backtongue. No specific study of the effectiveness of this oil in pellagra has been made; on the basis of general experience it seems unlikely that this oil contains the pellagra preventive in significant

amounts. *Beef muscle* is a good source of the preventive for both blacktongue and pellagra. *Pork liver* is a good source of the blacktongue preventive; it has not yet been studied in pellagra. *Canned salmon* contains the blacktongue preventive. A study of its effectiveness in pellagra is in progress. *Egg yolk* contains the blacktongue preventive; a specific study of its value in pellagra has not yet been undertaken. The canned *tomato* contains the preventive for both blacktongue and pellagra, but in relatively small amount. The *carrot* contains, but is a relatively poor source of, the preventive of blacktongue. Its reported failure in pellagra prevention is consistent with the indications of its feebleness as a blacktongue preventive. The *rutabaga* turnip contains, but is a relatively poor source of, the blacktongue preventive. Its failure in pellagra prevention is consistent with its poverty in the blacktongue preventive. So far as they have been studied, the foodstuffs that appear to be good sources of the blacktongue preventive also appear to be good sources of the pellagra preventive; those that appear to be poor sources of, or lacking in, the blacktongue preventive likewise appear to be poor sources of, or lacking in, the pellagra preventive. Considering the available evidence as a whole, it would seem highly probable, if not certain, that experimental blacktongue and pellagra are essentially identical conditions and thus that the preventive of blacktongue is identical with the pellagra preventive, or factor P-P. On the basis of the indications afforded by the test in the dog, liver, salmon, and egg yolk are recommended for use in the treatment and prevention of pellagra in the human being.

PHYSIOLOGY

PROCEEDINGS OF THE PHYSIOLOGICAL SOCIETY OF PHILADELPHIA

SESSION OF OCTOBER 15, 1928

The Mobility of Ions in Free Diffusion.—SAMUEL GOLDSCHMIDT, assisted by AMBROSE HUNSBERGER, JR. (from the Laboratory of Physiology of the University of Pennsylvania). The necessity of obtaining physical-chemical evidence which might decide whether certain processes of diffusion across the gut wall are due to forces arising within the solution, or are dependent upon the presence of a membrane (Goldschmidt, S., and Dayton, A.B., Goldschmidt, S., and Binger, C.; *Am. J. Physiol.*, 1919, **48**, 459,) has led us to a study of the factors which may modify the intrinsic mobility of ions in free diffusion.

Diffusion experiments with and without membranes have revealed that electrostatic forces arising from ionic charges are active in accelerating or retarding the movement of ions in aqueous solutions.

Comparative measurements of the rate of movement of Cl^- from aqueous solution in free diffusion, with its movement when other anions are added show: (1) No detectable change in the amount of Cl^- which passes in a unit of time when the added anion is univalent. A necessary condition for these comparisons is that the cations of the two salts either be the same, or, if different, that they possess the same intrinsic mobility. (2) An increase in the rate of diffusion of Cl^- when the added anion is divalent. (3) A still further increase in the rate of passage of Cl^- when the added anion is trivalent. (4) That this repellant effect of an ion of a given sign upon ions of the same sign, which is proportional to its degree of charge (valence), may be decreased by ions of the opposite sign in proportion to their charge (valence).

On the Mechanism of Opsonin and Bacteriotropin Action.—STUART MUDD, BALDUIN LUCKÉ, MORTON MCCUTCHEON and MAX STRUMIA (from the Department of Pathology, University of Pennsylvania). The present experiments represent the first stage of a study directed toward analysis of the mechanism of opsonin and bacteriotropin action in physical-chemical terms. They are intended to answer the question: "What changes do sera effect in bacteria in preparing them for phagocytosis?"

Immune sera have been prepared by injecting rabbits with Bacillus tuberculosis and a variety of related microörganisms. The bacteria, treated by serial dilutions of normal and immune sera, have been studied in the following reactions: (1) The bacteria remain in serum dilutions overnight and the degree of precipitation or agglutination is then read in each tube. (2) The serum-bacterial mixtures are strongly centrifugated and the sediments resuspended by shaking until the untreated tube shows an even suspension; the treated sediments resuspend in flocculi increasing in coarseness with their cohesiveness. (3) The bacteria are observed microscopically in an oil-water interface; before treatment with immune sera they pass readily into the oil; after treatment they resist passing into the oil. (4) The electrokinetic potential difference between the washed bacteria and their suspending medium is calculated from determinations in a microcataphoresis cell. These four reactions together give a picture of the surface properties of the bacteria. (5) Meanwhile mixtures of rabbit leukocytes with: (*a*) Bacteria and serum dilutions, or with (*b*) treated, washed bacteria are rotated in stoppered vials on a Robertson agitator. Smears are made from each mixture, stained, and the per cent of leukocytes which have taken up bacteria is recorded.

Sera reacting with bacteria of the tubercule-bacillus group cause agglutination, increased cohesion of the bacteria, reduced surface p. d., change from a bacterial surface readily wet by oil to a surface wet by water, and cause increased phagocytosis. The most important relationship thus far brought out is that in practically every instance in which an immune or normal serum has caused increased phagocytosis it has caused in approximately corresponding degree the above indicated changes in surface properties. Conversely when fresh, unheated rabbit sera have reacted with bacteria so as to produce the surface changes, corresponding increase in phagocytosis has uniformly resulted. The

sera of four rabbits have been followed by similar tests at weekly intervals during the course of active immunization by injection of bacteria. Striking correlation was found between the bacterial surface changes and the increase of phagocytosis produced by the sera of these animals.

However, when bacteria have been treated with aged or heated sera, the surface changes have been produced in a number of instances in which phagocytosis has failed. Moreover in series with aged sera phagocytosis in some instances reached a maximum not, as with the surface reactions, in the highest serum concentrations, but in serum concentrations as low as $\frac{1}{10}$ of 1 per cent. Finally, bacteria treated with normal human sera failed to cause phagocytosis by rabbit leukocytes, although marked surface changes were present.

These results are all consistent with the conclusion that the various surface reactions and phagocytosis are dependent upon combination with and deposition on the bacterial surface of serum components.

Probable Depth of Temperature End-organs in the Skin.—H. C. BAZETT, B. MCGLONE, and R. J. BROCKLEHURST (from the Laboratory of Physiology, University of Pennsylvania). Temperature changes within the dermis were determined by oblique needle thermocouples or by McGlone loop couples, and the thermal changes which accompany temperature sensations could in this way readily be measured. The forearm was supported. Either a warm or a cold sensitive spot was selected and the couples were sunk at varying depths beneath it. The spot was then stimulated with a 1.5 mm. metal point heated or cooled by irrigation with water. The point was applied by a rack and pinion. The temperature changes on the surface and at various depths were recorded photographically, and the durations of stimulation and sensation were signalled.

The rate of pentration of the temperature changes could be measured since these were delayed in proportion to the depth of the thermocouple. On graphic representation a fairly definite linear relationship is apparent The time corresponding to any depth is, however, rather variable; to some extent these variations appear dependent on the vascular conditions, so that the points are less scattered when the data obtained in cold and warm rooms, or obtained within the area of a histamine flare, are plotted separately. When so plotted those obtained in a cold environment are most regular. Under conditions of vascular dilatation the scattering is probably not mere experimental error, since it is particularly marked at a depth of about 2 mm., that is, at the junction of the dermis and subcutis; it is likely to be dependent partly on the anatomical arrangement of vessels, for it is impossible to apply the metal point so as to give equal pressure on the same bloodvessels on each repetition of the stimulus.

Vascular dilatation, whether produced by warmth or inflammation slows penetration to all depths in the case of a warm stimulus, and to the deeper part of the dermis when a cold stimulus is employed. In this deeper area the penetration of cold is slowed more than that of warmth. Penetration of cold in the more superficial layers is more complicated; it will be considered in connection with the sensation changes. In all

curves the penetration rate varied between 0.5 and 0.8 mm. per second. This velocity and the linear type of curve obtained suggest that the bloodflow in the smaller vessels is mainly concerned. The differences observed under varying conditions appear explicable as the result of changes in the thermal capacity and conductivity of the tissues caused by variations in vascular tone as the result of the environmental condition or the stimulus itself.

The latency of sensation also varied with the vascular condition and showed changes of the same type as those for penetration. For warmth latencies of 0.8 to 1.25 seconds were observed in cold and warm environments and within the area of a histamine flare. If 0.15 second be allowed for nervous processes (on a basis of comparison with touch and sound) then depths of 0.62 to 0.75 for the end organ for warmth may be estimated from the graph. The parallelism between changes in rate of conduction of heat and latency of sensation is marked and a depth of 0.8 ± 0.1 mm. may be provisionally assigned to this end organ.

The latencies for cold sensations were 0.3 second in a cold environment and within the area of a histamine flare; in a warm environment when needle thermocouples had been inserted it was about 0.5 second, but when loops had been threaded through the superficial layers 1.55 seconds. Comparison with the rate of penetration is difficult since short latencies imply a very superficial position for the end organ and penetration rates at such depths can only be estimated by inaccurate extrapolation.

There was, however, some parallelism; with loops the time of penetration of cold, like the latency of sensation, was longer in a warm room than either in a cold room or within the area of a histamine flare. In a warm room the time of penetration of cold was longer when loops were inserted than when oblique needles were used, but in this case the differences in rate of penetration could not account quantitatively for the very marked contrasts observed in latencies. The results suggest a depth of 0.2 ± 0.1 mm. for the end organ. Possibly the long latencies of sensation observed when loops were employed in a warm room indicate that capillary constriction is an essential precursor of a cold sensation, for under these conditions some inflammatory capillary dilatation is likely to have been present. The von Frey school has suggested that Krause's end bulbs give sensations of cold; they are described at about this depth.

Experiments on the Glomerular Elimination of Phenolsulphonephthalein and Indigo Carmine.—A. N. Richards and Arthur M. Walker (from the Laboratory of Pharmacology, University of Pennsylvania). Frogs' kidneys were perfused with an oxygenated mixture of equal parts of Hamburger's fluid and sterile normal horse serum, to which had been added a small amount of either phenolsulphonephthalein or indigo carmine. Glomerular fluid was collected during the perfusion and found to contain the dye in concentration equal to or higher than that in the perfusion fluid; whereas, when some of the same perfusion fluid was filtered through a collodion membrane, the concentration of dye in the filtrate was less than half that of the original fluid.

Reason was found for suspecting that small amounts of fluid might

be sucked back from tubule during the process of glomerular collection. Hence, another series was made similar to the first with the single exception that the lumen of the tubule was closed at a point close to the Malpighian body. In this series the concentration of dye in the glomerular fluid very closely approximated that of an ultrafiltrate.

A third series was made on living frogs. After subcutaneous injection of dye, the kidney was exposed and glomerular fluid collected after closure of its tubule. Samples of blood were taken repeatedly during the collection. Concentration of dye in glomerular fluid uniformly agreed with that of an ultrafiltrate from frog's plasma containing the average concentration of dye as determined by analysis of the blood samples taken.

The conclusion was reached that so far as the two dyes mentioned are concerned, the process of glomerular elimination is to be regarded as one of filtration through a membrane, impermeable to protein.

A fourth series of experiments was made which indicated that the volume of glomerular elimination is sufficient to account for all of the dye which a frog's kidney excretes.

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